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(54) Title: HUMAN PANCREAS AND PANCREATIC CANCER ASSOCIATED GENE SEQUENCES AND POLYPEPTIDES (57) Abstract This invention relates to newly identified pancreas or pancreatic cancer related polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "pancreatic cancer antigens", and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such pancreatic cancer antigens for detection, prevention and treatment of disorders of the pancreas, particularly the presence of pancreatic cancer. This invention relates to the pancreatic cancer antigens as well as vectors, host cells, antibodies directed to pancreatic cancer antigens and recombinant and synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing disorders related to the pancreas, including pancreatic cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of pancreatic cancer antigens of the invention. The present invention further relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.		

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Human Pancreas and Pancreatic Cancer Associated Gene Sequences and Polypeptides

5 *Field of the Invention*

This invention relates to newly identified pancreas or pancreatic cancer related polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "pancreatic cancer antigens," and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such pancreatic cancer
10 antigens for detection, prevention and treatment of disorders of the pancreas, particularly the presence of pancreatic cancer. This invention relates to the pancreatic cancer antigens as well as vectors, host cells, antibodies directed to pancreatic cancer antigens and recombinant and synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing disorders related to the pancreas,
15 including pancreatic cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of pancreatic cancer antigens of the invention. The present invention further relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.

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Background of the Invention

Cell growth is a carefully regulated process which responds to specific needs of the body. Occasionally, the intricate, and highly regulated controls dictating the rules for cellular division break down. When this occurs, the cell begins to grow and divide
25 independently of its homeostatic regulation resulting in a condition commonly referred to as cancer. In fact, cancer is the second leading cause of death among Americans aged 25-44.

Pancreatic cancer is one of the most dangerous cancers, killing half its victims within 6 weeks and having a 5-year survival rate of only 1%. The diagnosis of pancreatic carcinoma is often associated with a poor prognosis, because most patients already have advanced
30 disease. Despite the many advances reported during the past few years, pancreatic cancer remains a profound therapeutic challenge. It is hoped that the increasing knowledge of the

molecular biology of pancreatic carcinoma will lead to improvements in diagnosing, staging, and treating pancreatic adenocarcinoma (Brand et al., Curr Opin Oncol 10:362-6 (1998)).

There is a need, therefore, for identification and characterization of factors that modulate activation and differentiation of pancreatic cells, both normally and in disease states. In particular, there is a need to isolate and characterize additional molecules that mediate apoptosis, DNA repair, tumor-mediated angiogenesis, genetic imprinting, immune responses to tumors and tumor antigens and, among other things, that can play a role in detecting, preventing, ameliorating or correcting dysfunctions or diseases related to the pancreas.

Summary of the Invention

The present invention includes isolated nucleic acid molecules comprising, or alternatively, consisting of, a pancreas and/or pancreatic cancer associated polynucleotide sequence disclosed in the sequence listing (as SEQ ID NOs:1 to 459) and/or contained in a human cDNA clone described in Tables 1, 2 and 5 and deposited with the American Type Culture Collection ("ATCC"). Fragments, variant, and derivatives of these nucleic acid molecules are also encompassed by the invention. The present invention also includes isolated nucleic acid molecules comprising, or alternatively consisting of, a polynucleotide encoding a pancreas and/or pancreatic cancer polypeptide. The present invention further includes pancreas and/or pancreatic cancer polypeptides encoded by these polynucleotides. Further provided for are amino acid sequences comprising, or alternatively consisting of, pancreas and/or pancreatic cancer polypeptides as disclosed in the sequence listing (as SEQ ID NOs: 460 to 918) and/or encoded by a human cDNA clone described in Tables 1, 2 and 5 and deposited with the ATCC. Antibodies that bind these polypeptides are also encompassed by the invention. Polypeptide fragments, variants, and derivatives of these amino acid sequences are also encompassed by the invention, as are polynucleotides encoding these polypeptides and antibodies that bind these polypeptides. Also provided are diagnostic methods for diagnosing and treating, preventing, and/or prognosing disorders related to the pancreas, including pancreatic cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of pancreatic cancer antigens of the invention.

Detailed Description

Tables

Table 1 summarizes some of the pancreatic cancer antigens encompassed by the invention (including contig sequences (SEQ ID NO:X) and the cDNA clone related to the contig sequence) and further summarizes certain characteristics of the pancreatic cancer polynucleotides and the polypeptides encoded thereby. The first column shows the "SEQ ID NO:" for each of the 459 pancreatic cancer antigen polynucleotide sequences of the invention. The second column provides a unique "Sequence/Contig ID" identification for each pancreas and/or pancreatic cancer associated sequence. The third column, "Gene Name," and the fourth column, "Overlap," provide a putative identification of the gene based on the sequence similarity of its translation product to an amino acid sequence found in a publicly accessible gene database and the database accession no. for the database sequence having similarity, respectively. The fifth and sixth columns provide the location (nucleotide position nos. within the contig), "Start" and "End", in the polynucleotide sequence "SEQ ID NO:X" that delineate the preferred ORF shown in the sequence listing as SEQ ID NO:Y. The seventh and eighth columns provide the "% Identity" (percent identity) and "% Similarity" (percent similarity), respectively, observed between the aligned sequence segments of the translation product of SEQ ID NO:X and the database sequence. The ninth column provides a unique "Clone ID" for a cDNA clone related to each contig sequence.

Table 2 summarizes ATCC Deposits, Deposit dates, and ATCC designation numbers of deposits made with the ATCC in connection with the present application.

Table 3 indicates public ESTs, of which at least one, two, three, four, five, ten, fifteen or more of any one or more of these public EST sequences are optionally excluded from certain embodiments of the invention.

Table 4 lists residues comprising antigenic epitopes of antigenic epitope-bearing fragments present in most of the pancreas and/or pancreatic cancer associated polynucleotides described in Table 1 as predicted by the inventors using the algorithm of Jameson and Wolf, (1988) Comp. Appl. Biosci. 4:181-186. The Jameson-Wolf antigenic analysis was performed using the computer program PROTEAN (Version 3.11 for the Power Macintosh, DNASTAR, Inc., 1228 South Park Street Madison, WI). Pancreas and pancreatic cancer associated polypeptides (e.g., SEQ ID NO:Y, polypeptides encoded by SEQ ID NO:X,

or polypeptides encoded by the cDNA in the referenced cDNA clone) may possess one or more antigenic epitopes comprising residues described in Table 4. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly. The residues and locations shown in column two of Table 4 correspond to the amino acid sequences for most pancreas and/or pancreatic cancer associated polypeptide sequence shown in the Sequence Listing.

Table 5 shows the cDNA libraries sequenced, and ATCC designation numbers and vector information relating to these cDNA libraries.

Definitions

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X (as described in column 1 of Table 1) or the related cDNA clone (as described in column 9 of Table 1 and contained within a library deposited with the ATCC). For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having an amino acid sequence encoded by a polynucleotide of the invention as broadly defined (obviously

excluding poly-Phenylalanine or poly-Lysine peptide sequences which result from translation of a polyA tail of a sequence corresponding to a cDNA).

In the present invention, "SEQ ID NO:X" was often generated by overlapping sequences contained in multiple clones (contig analysis). A representative clone containing
5 all or most of the sequence for SEQ ID NO:X is deposited at Human Genome Sciences, Inc. (HGS) in a catalogued and archived library. As shown in column 9 of Table 1, each clone is identified by a cDNA Clone ID. Each Clone ID is unique to an individual clone and the Clone ID is all the information needed to retrieve a given clone from the HGS library. In addition to the individual cDNA clone deposits, most of the cDNA libraries from which the
10 clones were derived were deposited at the American Type Culture Collection (hereinafter "ATCC"). Table 5 provides a list of the deposited cDNA libraries. One can use the Clone ID to determine the library source by reference to Tables 2 and 5. Table 5 lists the deposited cDNA libraries by name and links each library to an ATCC Deposit. Library names contain four characters, for example, "HTWE." The name of a cDNA clone ("Clone ID") isolated
15 from that library begins with the same four characters, for example "HTWEP07". As mentioned below, Table 1 correlates the Clone ID names with SEQ ID NOs. Thus, starting with a SEQ ID NO, one can use Tables 1, 2 and 5 to determine the corresponding Clone ID, from which library it came and in which ATCC deposit the library is contained. Furthermore, it is possible to retrieve a given cDNA clone from the source library by techniques known in
20 the art and described elsewhere herein. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposits were made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for the purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides
25 capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, or the complement thereof (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein), and/or sequences contained in the related cDNA clone within a library deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50%
30 formamide, 5x SSC (750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65 degree C.

Also included within "polynucleotides" of the present invention are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH₂PO₄; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50 degree C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA⁺ sequences (such as any 3' terminal polyA⁺ tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

The polynucleotides of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or

RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

5 In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a
10 portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

15 "SEQ ID NO:X" refers to a pancreatic cancer antigen polynucleotide sequence described in Table 1. SEQ ID NO:X is identified by an integer specified in column 1 of Table 1. The polypeptide sequence SEQ ID NO:Y is a translated open reading frame (ORF) encoded by polynucleotide SEQ ID NO:X. There are 459 pancreatic cancer antigen polynucleotide sequences described in Table 1 and shown in the sequence listing (SEQ ID
20 NO:1 through SEQ ID NO:459). Likewise there are 459 polypeptide sequences shown in the sequence listing, one polypeptide sequence for each of the polynucleotide sequences (SEQ ID NO:460 through SEQ ID NO:918). The polynucleotide sequences are shown in the sequence listing immediately followed by all of the polypeptide sequences. Thus, a polypeptide sequence corresponding to polynucleotide sequence SEQ ID NO:1 is the first polypeptide
25 sequence shown in the sequence listing. The second polypeptide sequence corresponds to the polynucleotide sequence shown as SEQ ID NO:2, and so on. In otherwords, since there are 459 polynucleotide sequences, for any polynucleotide sequence SEQ ID NO:X, a corresponding polypeptide SEQ ID NO:Y can be determined by the formula $X + 459 = Y$. In addition, any of the unique "Sequence/Contig ID" defined in column 2 of Table 1, can be
30 linked to the corresponding polypeptide SEQ ID NO:Y by reference to Table 4.

The polypeptides of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may

contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

The pancreas and pancreatic cancer polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often

advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The pancreas and pancreatic cancer polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

"A polypeptide having functional activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular assay, such as, for example, a biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention).

The functional activity of the pancreatic cancer antigen polypeptides, and fragments, variants derivatives, and analogs thereof, can be assayed by various methods.

For example, in one embodiment where one is assaying for the ability to bind or compete with full-length polypeptide of the present invention for binding to an antibody to

the full length polypeptide antibody, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky, E., et al., Microbiol. Rev. 59:94-123 (1995). In another embodiment, physiological correlates polypeptide of the present invention binding to its substrates (signal transduction) can be assayed.

In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present invention and fragments, variants derivatives and analogs thereof to elicit polypeptide related biological activity (either in vitro or in vivo). Other methods will be known to the skilled artisan and are within the scope of the invention.

Pancreas and Pancreatic Cancer Associated Polynucleotides and Polypeptides of the Invention

It has been discovered herein that the polynucleotides described in Table 1 are expressed at significantly enhanced levels in human pancreas and/or pancreatic cancer tissues. Accordingly, such polynucleotides, polypeptides encoded by such polynucleotides,

and antibodies specific for such polypeptides find use in the prediction, diagnosis, prevention and treatment of pancreas related disorders, including pancreatic cancer as more fully described below.

5 Table 1 summarizes some of the polynucleotides encompassed by the invention (including contig sequences (SEQ ID NO:X) and the related cDNA clones) and further summarizes certain characteristics of these pancreas and/or pancreatic cancer associated polynucleotides and the polypeptides encoded thereby.

Table 1

Seq ID No.	Sequence/Contig ID	Gene Name	Overlap	HGS Nucleotide Start	HGS Nucleotide End	% Identity	% Similarity	Clone ID
1	456379	5'-AMP-activated protein kinase, gamma-1 subunit (Homo sapiens) >sp P54619 AAKG_HUMAN 5'-AMP-ACTIVATED PROTEIN KINASE, GAMMA-1 SUBUNIT (AMPK GAMMA-1 C11A1N). Length = 331	gil1335856	3	197	100	100	HCDAJ28
2	462108			2	1033			HHPDJ86
3	503446	Similarity to Yeast SOH-1 protein (SW:P38633) [Caenorhabditis elegans] >sp P91869 P91869 F32H2.2 PROTEIN. Length = 163	gnl P1D e1346272	161	415	66	80	HTTE140
4	507841			1	159			HQAA152
5	509287			1	480			IMTME61
6	509672	clk2-136, putative [Homo sapiens] >pir S53638 S53638 protein kinase clk2-139 (EC 2.7.1.-) - human Length = 139	gil632966	16	141	95	97	HTPAM31
7	509673			1	162			IMWBR61
8	518767			2	148			HTPBZ88
9	522008			1	378			HDPFN59
10	524112			248	475			HHPCN86
11	525971			1	579			HTXAR16

12	527156	ORF YOR262w [Saccharomyces cerevisiae] >pirS67159 S67159 probable membrane protein YOR262w - yeast (Saccharomyces cerevisiae) >sp Q08726 Q08726 CHROMOSOME XV READING FRAME ORF YOR262W. Length = 347	gn P D c252113	174	506	48	63	HMWF:W50
13	532502	electron transfer flavoprotein beta subunit [Homo sapiens] >pirS32482 S32482		73	267			HTPCP39
14	533459	electron transfer flavoprotein beta chain - human >sp P38117 ETFB_HUMAN ELECTRON TRANSFER FLAVOPROTEIN BETA-SUBUNIT (BETA-ETF). Length = 255	gi 297902	2	850	87	87	HKAAY56
15	533551	interleukin 4 receptor [Homo sapiens] >gi 3219334 (AC004525) Interleukin 4 alpha-chain precursor [Homo sapiens] >sp 24394 IL4R_HUMAN INTERLEUKIN-4 RECEPTOR ALPHA CHAIN PRECURSOR (IL-4R-ALPHA) (CD124 ANTIGEN). Length = 825	gi 33834	2	1564	84	84	HTOIEV80
16	537850	tetraspan membrane protein [Homo sapiens] >sp P48230 ILT4_HUMAN TETRASPAN MEMBRANE PROTEIN IL-TMP. Length = 202	gi 953239	179	913	89	89	III.DQN04
17	537925	sialyltransferase [Homo sapiens] >pirA54898 A54898 gal-beta1.3galNAc alpha-2,3-sialyltransferase (EC 2.4.99.-) human Length = 340	gi 522197	1	228	80	82	HSKYV64

18	538160	pancreatic zymogen granule membrane protein GP-2 [Homo sapiens] >pir G02091 G02091 pancreatic zymogen granule membrane protein GP-2 - human >sp P55259 GP2_HUMAN PANCREATIC SECRETORY GRANULE MEMBRANE MAJOR GLYCOPROTEIN GP2 PRECURSOR (PANCREATIC ZYMOGEN GRA	gil1244512	68	595	98	98	HIPWAR18
19	540420	Method: conceptual translation supplied by author; putative hybrid protein similar to HERV-H protease and HERV-E integrase [Human endogenous retrovirus] >sp Q68997 Q68997 SIMILAR TO HERV-H PROTEASE AND HERV-E INTEGRASE. >gil2587023 (AF026246) HERV-E integ	gil1049231	48	338	68	77	HTPBW19
20	540802	annexin III [Homo sapiens] >gil178697 1,2-cyclic-inositol-phosphate phosphodiesterase [Homo sapiens] >gil307115 lipocortin-III [Homo sapiens] >pir A47658 LUHU3 annexin III - human >sp P12429 ANX3_HUMAN ANNEXIN III (LIPOCORTIN III) (PLACENTAL ANTICOAGULANT	gil410202	198	671	99	99	IMEKCG44
21	540989	lipase related protein 1 [Homo sapiens] >pir A43357 A43357 pancreatic lipase-related protein 1 - human >sp P54315 LIP1_HUMAN PANCREATIC LIPASE RELATED PROTEIN 1 PRECURSOR (EC 3.1.1.3). Length = 467	gil187230	29	343	98	98	HPASD60

22	540997	lipase related protein 1 [Homo sapiens] >pir/A43357/A43357 pancreatic lipase-related protein 1 - human >spP54315/LIPT_HUMAN PANCREATIC LIPASE RELATED PROTEIN 1 PRECURSOR (EC 3.1.1.3). Length = 467	gil187230	2	409	98	99	IIPASC94
23	548735	P69 2-3A synthase II - human Length = 727	pir B42665 B42665	101	604	96	98	IIMTAE33
24	549709	cytochrome P450 PCN3 [Homo sapiens] >pir/A34101/A34101 cytochrome P450 3A5 - human >spP20815/CP35_HUMAN CYTOCHROME P450 3A5 (EC 1.14.14.1) (CYP11A5) (P450-PCN3). >gil950342 cytochrome P450 [Homo sapiens] (SUB 1-24) Length = 502	gil181346	72	305	64	64	IHSBZ89
25	550007	thimet oligopeptidase [Homo sapiens] >gil1030055 metalloproteinase [Homo sapiens] >pir C4197 HYTH1 thimet oligopeptidase (EC 3.4.24.15) - human >spP52888/MEPD_HUMAN THIMET OLIGOPEPTIDASE (EC 3.4.24.15) (ENDOPEPTIDASE 24.15) (MP78). (SUB 2-689) Length =	gil1098600	150	782	100	100	HCEIB78

26	550118	macrophage capping protein [Homo sapiens] >pir A43358 A43358 macrophage capping protein - human >sp P4012 CAPG_HUMAN MACROPHAGE_CAPPING_PROTEIN (ACTIN-REGULATORY PROTEIN CAP- G). >gi 515505 Cap-G [Homo sapiens] {SUB 1-172} Length = 348	gi 187456	1	1113	99	99	IIDPXJ18
27	550148	carbonic anhydrase IV [Homo sapiens] >pir A45745 CRH104 carbonic dehydratase (EC: 4.2.1.1) IV precursor - human	274	456				IIISBA17
28	550870	>sp P22748 CAH4_HUMAN CARBONIC ANHYDRASE IV PRECURSOR (EC 4.2.1.1) (CARBONATE DEHYDRATASE IV). Length = 312	1	594	94	94		IINFIA35
29	552506	preproglucagon [Homo sapiens] >pir A24377 GCHU glucagon precursor - human >sp P01275 GLUC_HUMAN GLUCAGON PRECURSOR. >gi 31778 Human gene encoding preproglucagon. Glucagon is a 29-amino acid pancreatic hormone which counteracts the blood glucose-lowering a	gi 183270	3	350	96	96	IITPD178

30	553765	complement factor B [Homo sapiens] >pir S34075 B3111 complement factor B precursor - human >sp P00751 CFAB_HUMAN COMPLEMENT FACTOR B PRECURSOR (EC 3.4.21.47) (C3/C5 CONVERTASE) (PROPERDIN FACTOR B) (GLYCINE- RICH BETA GLYCOPROTEIN) (GBC) (PBF2). >gi 758090	48	1214	100	100	III.DIKK20
31	554050	histidyl-tRNA synthetase [Homo sapiens] >pir 37559 SYHUHT histidine--tRNA ligase (EC 6.1.1.21) - human >gi 431312 histidyl tRNA synthetase [Homo sapiens] {SUB 1-30; Length = 509	374	934	86	86	HARME85
32	554186	brain glycogen phosphorylase [Homo sapiens] >pir A29949 A29949 glycogen phosphorylase (EC 2.4.1.1), brain (astrocytoma cell line) - human Length = 863	2	814	98	99	HKACY69
33	554716	transcobalamin 1 precursor [Homo sapiens] >pir A34227 A34227 transcobalamin 1 precursor - human Length = 433	1	441	97	97	HCHAC67
34	556791	integrin alpha 1 subunit - human (fragment) >sp P56199 ITAI_HUMAN INTEGRIN ALPHA-1 (LAMININ AND COLLAGEN RECEPTOR) (VLA-1) (CD49A). Length = 1151	2	484	93	93	HFIYR48

35	557121	gamma-glutamyl transpeptidase-related protein [Homo sapiens] >pir A41125 A41125 gamma-glutamyl transferase (EC 2.3.2.2) related protein - human >sp P36269 GGT5_HUMAN GAMMA-GLUTAMYL TRANSPEPTIDASE 5 PRECURSOR (EC 2.3.2.2) (GAMMA-GLUTAMYLTRANSFERASE 5) (GGT-R	gil183142	151	567	100	100	115C1.81
36	557199	180 kDa bullous pemphigoid antigen 2/type XVII collagen [Homo sapiens] >sp E307563 E307563 180 KDA BULLOUS PEMPHIGOID ANTIGEN 2/TYPE XVII COLLAGEN. >sp G1877435 G1877435 180 KDA BULLOUS PEMPHIGOID ANTIGEN 2/TYPE XVII COLLAGEN. Length = 1497	gil1877435	2	646	81	81	HPDDA57
37	557293	alpha-5 type IV collagen [Homo sapiens] >gil180825 collagen type IV alpha 5 chain [Homo sapiens] {SUB 833-1604} Length = 1604	gil1314210	3	929	99	99	HISB190
38	557441	neurofibromin [Rattus norvegicus] >pir JC5196 JC5196 neurofibromin 1 - rat >sp P97526 P97526 NEUROFIBROMIN. >gil309451 neurofibromin [Mus musculus] {SUB 1-96} >gil1084091 neurofibromatosis 1 [Homo sapiens] {SUB 97-161} >gil1084092 neurofibromatosis 1 [Homo	gnlPID d1008732	207	326	100	100	HTPAD51

39	558091	flavin-containing monooxygenase 5 [Homo sapiens] >pir[S71618]S71618 dimethylamine monooxygenase (N-oxide-forming) (EC 1.14.13.8) FMO5 - human >sp P49326 FMO5_HUMAN DIMETHYLAMINE MONOOXYGENASE [N-OXIDE FORMING] 5 (EC 1.14.13.8) (HEPATIC FLAVIN-CONTAINING	gil559046	803	1066	98	98	11E9CK194
40	558423	translin [Homo sapiens] >pir[S51738]S51738 translin - human >sp Q15631 Q15631 TRANSLIN. >gn P1D1c3 3773 MTRANCDS [Homo sapiens] ; SUB 23-215; Length = 228	gil607130	49	807	93	93	11D1DF09
41	558465	G/T mismatch-specific thymine DNA glycosylase [Homo sapiens] Length = 410	gil1378107	1	507	90	91	11AMFJ55
42	558493	tubulin beta-1 chain - slime mold (Physarum polycephalum) (fragment) >gil 313801 beta-tubulin [Physarum polycephalum] ; SUB 1-203; Length = 204	pir[S02532]S02532	1	357	76	86	11TTEJ40
43	558778	T-cell antigen receptor (AA 1 - 292) [Homo sapiens] >pir[S03421]S03421 T-cell receptor delta chain precursor (Peer) - human Length = 292	gil37004	290	625	95	95	11SIDP61
44	558818	tRNA-Guanine Transglycosylase [Homo sapiens] >pir[G01932]G01932 tRNA-Guanine Transglycosylase - human Length = 494	gil940182	1	468	100	100	11PIBT63

45	563182	(AF072128) claudin-2 [Mus musculus] >sp O88552 O88552 CLAUDIN-2. Length = 230	gi 33335184	2	466	81	85	HCIMQ60
46	572571			194	553			HAICW02
47	575525	Bat2 [Homo sapiens] >pir S3767 S37671 bat2 protein - human Length = 1870	gi 29375	553	858	85	87	HAPOJ89
48	580659			695	1003			HBICR03
49	583650	islet regenerating protein [Homo sapiens] >pir A35197 RGHUIA regenerating islet lectin 1-alpha precursor - human >sp P05451 LITA_HUMAN LITHIOSTATINE 1 ALPHA PRECURSOR (PANCREATIC STONE PROTEIN) (PSP) (PANCREATIC THREAD PROTEIN) (PTP) (ISLET OF LANGERHANS	gi 190979	261	413	78	83	HTPDS26
50	584698			982	1200			HLQCJ79
51	585791	B61 [Homo sapiens] >pir A36377 A36377 B61 protein precursor - human >sp P20827 EFA1_HUMAN EPHRIN-A1 PRECURSOR (EPH-RELATED RECEPTOR TYROSINE KINASE LIGAND 1) (LERK-1) (IMMEDIATE EARLY RESPONSE PROTEIN B61) (TUMOR NECROSIS FACTOR ALPHA- INDUCED PROTEIN 4)	gi 179321	52	705	95	95	HSDT08

52	587229	phospholipase [Homo sapiens] >gi 387025 phospholipase [Homo sapiens] >gi 2769697 (AC003982) Phosphatidylcholine 2- acylglycerolase [Homo sapiens] >pir C25793 PSTU phospholipase A2 (EC 3.1.1.4) precursor, pancreatic - human >sp P04054 PA21_HUMAN PHOSPHOLIPASE	gi 190013	3	470	81	81	11PDIIP22
53	587246	probable transmembrane protein TMC - human Length = 705	pir S70029 S70029	67	573	92	92	111.WAF93
54	587486	alpha-subunit of prolyl 4-hydroxylase [Homo sapiens] >pir 37173 DAIHUA2 procollagen-proline dioxygenase (EC 1.14.11.2) alpha chain precursor, splice form 2 - human >sp P13674 P4HA_HUMAN PROLYL 4-HYDROXYLASE ALPHA SUBUNIT PRECURSOR (EC 1.14.11.2). Length =	gi 602675	745	1734	95	95	11DPWQ32
55	589218	adenyl cyclase [Homo sapiens] >gi 395275		6	185			HBSAL59
56	592154	adenylate cyclase [Homo sapiens] >pir 37136 37136 adenylate cyclase (EC 4.6.1.1) - human (fragment) >sp Q08462 CYA2_HUMAN ADENYLATE CYCLASE, TYPE II (EC 4.6.1.1) (ATP PYROPHOSPHATE- LYASE) (ADENYL CYCLASE) (FR	gi 763444	101	1033	95	95	HAAOAF42

57	598664	unnamed protein product [unidentified] >gil35330 carboxypeptidase a [Homo sapiens] >pir[S29127/S29127 carboxypeptidase A (EC 3.4.17.1) CPA1 precursor - human >sp P15085 CBP1_HUMAN CARBOXYPEPTIDASE A1 PRECURSOR (EC 3.4.17.1). Length = 419	gnl PID e307065	1	255	97	97	HTPD006
58	598665	unnamed protein product [unidentified] >gil35330 carboxypeptidase a [Homo sapiens] >pir[S29127/S29127 carboxypeptidase A (EC 3.4.17.1) CPA1 precursor - human >sp P15085 CBP1_HUMAN CARBOXYPEPTIDASE A1 PRECURSOR (EC 3.4.17.1). Length = 419	gnl PID e307065	1	1218	100	100	HTPEL79
59	604719	ADP-ribosylation factor [Bos taurus] >gil178156 ADP-ribosylation factor 1 [Homo sapiens] >gil178164 ADP-ribosylation factor 1 [Homo sapiens]	gil162627	1	651	100	100	HSHCL62
60	612689			243	578			IIMADQ02
61	612980			47	259			HISAD74
62	615134	metavinculin - pig (fragments) >gil2283 metavinculin [Sus scrofa] {SUB 113-336} Length = 336	pir[S29507/S29507	30	578	100	100	IIAIIIE20
63	616064			159	398			HASCD63

64	616096	(AC004877) sco-spondin-mucin-like; similar to P98167 (PID:g1711548); details of intron/exon structure uncertain [Homo sapiens] >sp O75851 O75851 WUGSC:H_DJ0751113.1 PROTEIN (FRAGMENT). Length = 4123	gil3638957	99	221	40	52	HHHCQ05
65	616926	Gps2 [Homo sapiens] Length = 327						
66	634923	islet regenerating protein [Homo sapiens] >pir A35197 RGHUA regenerating islet lectin 1-alpha precursor - human >sp P05451 LITA_HUMAN LITHOSTATHINE 1 ALPHA PRECURSOR (PANCREATIC STONE PROTEIN) (PSP) (PANCREATIC THREAD PROTEIN) (PTP) (ISLET OF LANGERHANS	gil1049070 gil190979	2 148	1123 447	100 81	100 88	HHDPJK81 HHDPBT17
67	646688	ORF1 [Homo sapiens] >sp Q14921 Q14921 NONSPECIFIC CROSSREACTING ANTIGEN. Length = 100	gil189086	508	819	99	99	HHDPDY03
68	647531	calcium-dependent protease [Oryctolagus cuniculus] >pir B24815 B24815 calpain (EC 3.4.22.17) large chain 2 - rabbit (fragment) >sp P06814 CAN2_RABBIT CALPAIN 2; LARGE [CATALYTIC] SUBUNIT (EC 3.4.22.17) [CALCIUM-ACTIVATED NEUTRAL PROTEINASE] (CANP) (M-TYPE)	gil165666	809	1177	76	81	HMSCC36

69	647695	preprocarboxypeptidase A2 [Homo sapiens] >pirA5617 A5617 carboxypeptidase A2 (EC 3.4.17.15) precursor - human >sp P48052 C1PA2_HUMAN CARBOXYPEPTIDASE A2 PRECURSOR (EC 3.4.17.15). Length = 417	gi 790227	2	1285	92	92	HVAAAB38
70	647699	chymotrypsin-like protease CTRL-1 [Homo sapiens] >gi 406228 chymotrypsin-like protease CTRL-1 [Homo sapiens] >pir 38136 38136 chymotrypsin-like protease (EC 3.4.21.-) CTRL-1 - human >sp P40313 CTRL_HUMAN CHYMOTRYPSIN-LIKE PROTEASE CTRL-1 PRECURSOR (EC	gi 438039	2	577	100	100	IICCMIB81
71	651706	erythrocyte p55 [Homo sapiens] >sp Q00013 EM55_HUMAN 55 KD ERYTHROCYTE MEMBRANE PROTEIN (P55). Length = 466	gi 189786	1	963	96	97	IITIC011
72	651726	arylamidase deacetylase [Homo sapiens] >pir A53856 A53856 aryl-acylamidase (EC 3.5.1.13) - human >sp P22760 AAAD_HUMAN ARYLAMIDE DEACETYLASE (EC 3.5.1.13) (AAADAC). [SUB 2-399] Length = 399	gi 537514	384	1553	99	99	HPV11.70
73	652160	alpha 2-macroglobulin 690-730 [Homo sapiens] Length = 1474	gi 579592	78	860	92	92	IIDPUB04
74	654015			172	390			IISAV29

75	656339	alpha endosulfine [Homo sapiens] >sp O43768 O43768 ALPHA ENDOSULFINE. >gnl P1D c224652 alpha endosulfine [Bos taurus] {SUB 25-101} Length = 121	gnl P1D c284090	1	450	100	100	100	IKGCM36
76	657190			293	493				HLT1143
77	657859			3	323				HNKAA14
78	662143			576	722				HLDQI35
79	662212	FK506 polyketide synthase [Streptomyces sp.] >sp P95814 P95814 FK506 POLYKETIDE SYNTHASE. Length = 6420	gnl P1D c290681	11	457	45	59		HHPAG88
80	662225			107	289				HWACN48
81	662496			3	446				HWIHC17
82	669529			254	343				HHSBT20
83	670453	acid sphingomyelinase [Homo sapiens] >sp Q16837 Q16837 ACID SPHINGOMYELINASE (EC 3.1.4.12) (SPHINGOMYELIN PHOSPHODIESTERASE) (NEUTRAL SPHINGOMYELINASE). >gi 972770 acid sphingomyelinase [Homo sapiens] {SUB 33- 629} Length = 629	gi 972769	926	1648	100	100		HNAJQ46
84	675028	seven in absentia homolog [Homo sapiens] >gi 2673966 hsIAH1 [Homo sapiens] >sp O43269 O43269 hsIAH1. Length = 282	gi 3041825	18	284	100	100		HIE2109
85	681325			3	224				HAJBC26
86	683103			212	1024				HITBN65

87	684432	serine hydroxymethyltransferase [Homo sapiens] >gi307422 serine hydroxymethyltransferase [Homo sapiens] >pirA46746/A46746 glycine hydroxymethyltransferase (EC 2.1.2.1), cytosolic - human >spP34896/GLYC_HUMAN SERINE HYDROXYMETHYLTRANSFERASE, CYTOSOLIC (gi338636	3	905	94	95	1151^A^79
88	688018	protease (put.): putative [Simian immunodeficiency virus] >spQ85727/Q85727 PIGTAILED MONKEY SIMIAN T-CELL LEUKEMIA VIRUS PROTEASE (FRAGMENT). Length = 215	gi334735	169	351	66	77	1117PDE05
89	688077	(AF047440) ribosomal protein L33-like protein [Homo sapiens] >spQ75394/Q75394 RIBOSOMAL PROTEIN L33-LIKE PROTEIN. Length = 65	gi3335136	1	276	100	100	111EBAG86
90	691522	similar to vacuolar biogenesis protein (pnp5): cDNA EST EMBL:D27614 comes from this gene; cDNA EST EMBL:D34974 comes from this gene [Caenorhabditis elegans] >gnlP1Djc1351725 similar to vacuolar biogenesis protein (pnp5): cDNA EST EMBL:D27614 comes from t	gnlP1Djc1351725	1	1179	32	54	111TACN89

91	693706	transcription factor ISGF-3 [Homo sapiens] >sp G228107 IG228107 TRANSCRIPTION FACTOR ISGF-3. >sp G116808 G116808 SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION 1A. STAT1A=INTERLEUKIN-6 RESPONSE ELEMENT BINDING PROTEIN [SRC- HOMOLOGY DOMAIN TYPE 2]. [S	gil2281071	184	2541	98	98	HAICK36
92	694523			1	204			HTPDK30
93	697517	PHOSPHOGLUCOMUTASE (EC 5.4.2.2) (GLUCOSE PHOSPHOMUTASE) (PGM). Length = 561	sp P36871 PGMU_HU MAN	117	1649	91	91	HUBDL34
94	699054			338	889			HMECT29
95	699464			2	241			HTLDA39
96	703402	(AF000422) TTF-1 interacting peptide 5 [Homo sapiens] >sp O00536 O00536 TTF-1 INTERACTING PEPTIDE 5 (FRAGMENT). Length = 407	gil2183083	1	423	94	95	HHEIV36
97	703651	guanine nucleotide-binding protein alpha subunit, G alpha 12 - human >sp G264227 G264227 GUANINE NUCLEOTIDE-BINDING PROTEIN ALPHA SUBUNIT, G ALPHA 12. Length = 381	pir A48071 A48071	3	332	99	99	HDPGIN16
98	704905			359	655			HPMFK19
99	706907			1	153			HRSAR67

100	708515	CDM [Homo sapiens] >gil535058 tumor-associated antigen [Homo sapiens] >gil508820 CDM protein [Homo sapiens] >pir[S4279]S44279 CDM protein - human >sp P51572 CDM_HUMAN CDM PROTEIN (6C6-AG TUMOR-ASSOCIATED ANTIGEN) (DXS1357E) >gil1020320 CDM protein [Hom	gil479157	1	480	87	87	HCT116A53
101	710572			6	248			H1H1ASC40
102	710618			125	325			H1BMAC72
103	711810			283	543			H1BXC783
104	714933	RNA adenosine deaminase [Homo sapiens] >sp O43859 O43859 RNA ADENOSINE DEAMINASE. Length = 1181	gil2795790	2	370	89	90	H1AMFQ09
105	716331	(A1006621) embryonic lung protein [Homo sapiens] >sp G2654559 G2654559 EMBRYONIC LUNG PROTEIN. Length = 568	gil2654559	1	564	91	91	H1LTHP10
106	717686			282	494			H1TPBX62
107	718187			1	153			H1TPDG49
108	719934	triglyceride lipase precursor [Homo sapiens] >gil1304379 pancreatic lipase [Homo sapiens] >pir C43357 C43357 triacylglycerol lipase (EC 3.1.1.3) precursor, pancreatic - human >sp P16233 LIPP_HUMAN TRIACYLGLYCEROL LIPASE PR	gil339597	2	1420	100	100	H1PASD23

109	722980	plasma gelsolin precursor [Sus scrofa] >gi758306 gelsolin [Sus scrofa] >pir[S02665]S02665 gelsolin precursor - pig (fragment) >sp[P20305]GELS_PIG GELSOLIN PRECURSOR, PLASMA (ACTIN-DEPOLYMERIZING FACTOR) (ADF) (BREVIN) (FRAGMENT). Length = 772	gi164472	67	375	100	100	100	III.QC.T60
110	723596	poly(A) binding protein [Mus musculus] >pir[48718]48718 poly(A) binding protein - mouse >sp[P2934]PAB1_MOUSE POLYADENYLATE-BINDING PROTEIN 1 (POLY(A) BINDING PROTEIN 1) (PABP 1). Length = 636	gi153754	1010	1225	61	67	67	HTTDR30
111	724352	(A1225089) 2'-5' oligoadenylate synthetase (p59OAS) [Homo sapiens] >sp[O75686]O75686 2'-5' OLIGOADENYLATE SYNTHETASE (P59OAS). Length = 514	gnl P10 c1316607	255	662				HK.GBC30
112	724430			311	547				HMW.CX50
113	724855			3	440				IIPIK.80
114	724904			1	417	100	100	100	IT13.TB04
115	725642	synaptotagmin VI [Rattus norvegicus] >pir[S38399]S38399 celluagmin I synVI - rat >sp[Q62746]Q62746 SYNAPTOTAGMIN VI. Length = 511	gi1643654	1	303	85	86	86	IIISBX52
116	726192	Highly similar to murine eps 15 G.B.A.N. L221768 [Homo sapiens] >pir[S43074]S43074 AF-1p protein - human Length = 896	gi1470035	276	785	79	79	79	IIISKX1103

117	726964	elastase 2 precursor [Homo sapiens] >gil182058 pancreatic elastase II/A zymogen [Homo sapiens] >pir1P26823 B26823 pancreatic elastase II (EC 3.4.21.71) A precursor - human >sp P08217 EL2A_HUMAN E:LASTASE 2A PRECURSOR (EC 3.4.21.71). Length = 269	gil182023	2	808	92	92	11P/AS177
118	730930	glutathione synthetase [Homo sapiens] >gil1236350 glutathione synthetase [Homo sapiens] >pir S56748 S56748 glutathione synthase (EC 6.3.2.3), brain - human >sp P48637 CSH1B_HUMAN GLUTATHIONE SYNTHETASE (EC 6.3.2.3) (GLUTATHIONE SYNTHASE) (GSH SYNTHETASE) (gil1886284	22	1530	97	97	III.WBL10
119	731314	(AF029786) GBAS [Homo sapiens] >sp O75323 O75323 GBAS. Length = 286	gil3403167	91	261	100	100	IISPAK79
120	732386			3	632			HLTDQ55
121	732909			759	1220			III.TCA26
122	733088			1	399			IIADEY44
123	733351			287	463			HDPC1.56
124	733693			1	276			IIITPDI59
125	734760	(AF042379) spindle pole body protein spc97 homolog GCP2 [Homo sapiens] >sp O43632 O43632 SPINDLE POLE BODY PROTEIN SPC97 HOMOLOG. Length = 902	gil2801701	205	1584	96	96	III.MEUG8
126	735711	glutamate pyruvate transaminase [Homo sapiens] Length = 496	gil1763096	12	842	66	82	II2CB161

127	742413	common fibrinogen alpha chain [Homo sapiens] >gi 182426 A-alpha fibrinogen [Homo sapiens] >gi 4033511 fibrinogen alpha subunit [Homo sapiens] >pir A93956 FGHUA fibrinogen alpha chain precursor, short splice form - human >gi 532482 alpha-fibrinogen [Homo s	gi 458554	3	779			IIFTAS62
128	742676			2	1081	89	89	IIIICN22
129	742781	syntaxin 7 [Homo sapiens] Length = 261	gi 2337920	344	607			IIIE8AY14
130	743356			173	298			IIICFDA89
131	745694			1	105			IIIEIHK36
132	747235			63	743			IIIEBFI18
133	750986			156	689	83	83	IIILQUR21
134	751068	pro-alpha-1 type V collagen [Homo sapiens] >pir S18802 CGHUIV collagen alpha 1(V) chain precursor - human >sp Q15094 Q15094 PRO-ALPHA-1 TYPE I VCOLLAGEN Length = 1838	gi 189520	529	810			IIIRABQ88
135	751164			1341	1736			IIIE3G96
136	751890			18	308			IIITPBR05
137	751991			1	1530			IIIMSIS33
138	752449			1	270			IIILYDM55
139	752504			1	552	94	95	IIIOUDR20

140	752688	(AF006088) p16-Arc [Homo sapiens] >gi2407611 (AF017807) Arp2/3 complex 16kDa subunit [Homo sapiens] >sp O15511 AR16_HUMAN ARP2/3 COMPLEX 16 KD SUBUNIT (P16-ARC). Length = 151	gi2282042	140	451	100	100	HEBCK82
141	752889	testican [Homo sapiens] >sp Q08629 Q08629 TESTICAN PRECURSOR. >gi2282168 (AC005213) testican [Homo sapiens] {SUB 237-439} Length = 439	gi793845	153	518	87	87	HEEDN77
142	753150	pre-mRNA splicing factor [Homo sapiens] >pir A48133 A48133 pre-mRNA splicing SRp75 - human >gi2914669 (AC004236) SRP40011.1 [Homo sapiens] {SUB 1-192} Length = 494	gi307438	259	1176	100	100	HELIHM06
143	753690	(AL031058) dJ512B11.1 (Desmoplakin 1 (DPI)) [Homo sapiens] >sp O75993 O75993 DJ512B11.1 (DESMOPLAKIN 1 (DPI)). Length = 2871	gnl PIDc1329910	246	743	87	87	HHHBC69
144	754479			160	543			HHSDF69
145	754692			338	2122			HTTBL33

146	756814	glucose transporter glycoprotein [Homo sapiens] >pirA27217/A27217 glucose transport protein - human >sp P11166 GTR1_HUMAN GLUCOSE TRANSPORTER TYPE 1, ERYTHROCYTE/BRAIN. >hbs 77925 glucose transporter isoform 1, GLUT1 [mice, embryo, Peptide Partial, 107	g 1183303	44	679	90	90	11CWB185
147	757127	(A1010046) guanine nucleotide-exchange factor [Homo sapiens]		253	501			11BAFN70
148	757347	>sp E1363645 E1363645 GUANINE NUCLEOTIDE-EXCHANGE FACTOR. Length = 548	gn P1D1e1363645	213	620			11MSFX70
149	757495			88	1221	99	100	11TTPY44
150	757715	(A1008986) similar to tyrosine-protein kinase [Caenorhabditis elegans] >gn P1D1e1348186 similar to tyrosine-protein kinase [Caenorhabditis elegans] >sp Q45668 Q45668 1137N21.1 PROTEIN. Length = 231	gn P1D1e1347680	227	1729	72	84	11EBFD01
151	760388			2	232			11LWA1126
152	760433	mutant sterol regulatory element binding protein-2 [Cricketulus griseus] Length = 839	g 841318	2	730	83	89	11BIDG86
153	760545	(A1051426) slow delayed rectifier channel subunit [Homo sapiens] >sp O60607 O60607 SLOW DELAYED RECTIFIER CHANNEL1, SUBUNIT. Length = 548	g 2961249	1	345	80	81	11SSF506

154	761566	protein tyrosine phosphatase PTPCAAX1 [Homo sapiens] >gi 2961199 (AF051160) tyrosine phosphatase [Homo sapiens] >gi 530162 tyrosine phosphatase [Rattus rattus] >gi 1814024 protein tyrosine phosphatase [Mus musculus] >pir A56059/A56059 protein-tyrosine-pho	gi 1777755	601	1125	99	99	110POW14
155	761740	colipase precursor [Homo sapiens] >gi 1483624 colipase [Homo sapiens] >pir A42568/XI.HU colipase precursor - human >sp P04118/COL_HUMAN COLIPASE PRECURSOR. Length = 112	gi 180886	7 25	435 417	86	86	HSIFY01 HTPCY18
157	765428	(AF050640) NADH-ubiquinone oxidoreductase NDUFS2 subunit [Homo sapiens] >sp G3337443/G3337443 NADH- UBIQUINONE OXIDOREDUCTASE NDUFS2 SUBUNIT. Length = 463	gi 3337443	142 38 2	627 901 568	87	89	HL.YC190 HINTIP54 HISKNC05
158	766686							
159	767396							
160	767501	L-arginine:glycine amidinotransferase [EC 2.1.4.1] [human, kidney carcinoma cells, Peptide, 423 aa] [Homo sapiens] >pir S41734/S41734 glycine amidinotransferase (EC 2.1.4.1) precursor - human >sp P50440/GATM_HUMAN GLYCINE AMIDINOTRANSFERASE PRECURSOR (EC	hbs 143982	1	735	95	95	IKKIMB02

161	767945		183	302			IIHSEB76
162	768996		209	454			IIHPCQ34
163	771415		1	747			IIHENW77
164	772657	zygini1 [Rattus norvegicus] >sp P97578 P97578_ZYGINI1 (FRAGMENT). Length = 324	110	1087	69	72	IIHQEV69
165	773123	beta-polymerase [Homo sapiens] >gi 553614 polymerase beta [Homo sapiens] {SUB 1- 39} Length = 335	278	1012	35	58	IIWIIIN55
166	773193		246	695			IIHODD78
167	773710		3	707			IIFTYK62
168	774283	(A1047384) postsynaptic protein CRIP1 [Rattus norvegicus] >sp O70333 O70333 POSTSYNAPTIC PROTEIN CRIP1. Length = 101	3	395	99	99	IIATCT32
169	774369		33	224			IIIDAAC66
170	774754	(A1013758) polyadenylate binding protein- interacting protein-1 [Homo sapiens] >sp O60455 O60455_POLYADENYLATE BINDING PROTEIN-INTERACTING PROTEIN-1. Length = 480	52	1239	92	92	IIEBON42
171	774823	out at first [Drosophila virilis] >sp O18638 O18638_OUT_AT_FIRST. Length = 305	2	568	46	62	IIIMKE85
172	775510		3	98			IIIVAMK80
173	775634		106	537			IIITXB191
174	775640		53	358			IIITWDN88
175	775802		762	971			IIJMAF44

176	777470	Nr1-1 [Homo sapiens] >pir C4014 C4014 steroid hormone-nuclear receptor NR - human >sp 55055 NER_HUMAN NUCLEAR RECEPTOR NER (UBIQUITOUSLY-EXPRESSED NUCLEAR RECEPTOR) >gil608135 orphan receptor [Homo sapiens] {SUB 7- 461} Length = 461	gil641962	731	1621	91	91	111ACM37
177	777652	(AF053091) eyelid [Drosophila melanogaster] >sp O61603 O61603 EYELID. Length = 2715		2	340			IIDPV110
178	778998			197	409			IIISCO10
179	779273		gil2981221	1	699	51	67	IIKADK51
180	779297	cek5 receptor ligand [Mus musculus] Length = 345	gil575929	1	318	100	100	IICTHH53
181	779664	enhancer-trap-focus-1 [Mus musculus] >pir A56559 A56559 enhancer-trap-focus-1 protein - mouse (fragment) >sp Q04692 Q04692 ENHANCER TRAP LOCUS 1 (ENHANCER-TRAP-LOCUS 1 PROTEIN) (FRAGMENT). Length = 1136	gil50866	184	675	98	99	IIISC182
182	780565	preprochymotrypsinogen (EC 3.4.21.1) [Homo sapiens] >pir A31299 A31299 chymotrypsin (EC 3.4.21.1) precursor - human >sp P17538 CTRB_HUMAN CHYMOTRYPSINOGEN B PRECURSOR (EC 3.4.21.1). Length = 263	gil181190	10	144			IIISDJ93
183	780665			3	401	100	100	IIIVANF29

184	780666	preprochymotrypsinogen (EC 3.4.21.1) [Homo sapiens] >pir A31299 A31299 chymotrypsin (EC 3.4.21.1) precursor - human >sp P17538 CTRB_HUMAN CHYMOTRYPSINOGEN B PRECURSOR (EC 3.4.21.1). Length = 263	gi 181190	57	494	91	93	HTTPD51
185	781579	26S proteasome regulatory chain 12 - human Length = 321	pir S6549 S65491	56	1102	94	94	HLWB170
186	782052	(AF000002) 376aa long hypothetical dehydrogenase [Pyrococcus horikoshii] >sp O58320 O58320_376AA LONG HYPOTHETICAL DEHYDROGENASE. Length = 376	gn P D d1030629	76	447	35	58	HIISDQ77
187	782393	(AF068195) putative glioblastoma cell differentiation-related protein [Homo sapiens] >sp O75500 O75500 PUTATIVE GLIOBLASTOMA CELL DIFFERENTIATION-RELATED PROTEIN. Length = 334	gi 3211975	685	1392	86	86	HIISFC84 HIISFR96 HFXJX12 HIDPIZ33
188	782907							
189	783220							
190	783300							
191	783938	(AF068195) putative glioblastoma cell differentiation-related protein [Homo sapiens] >sp O75500 O75500 PUTATIVE GLIOBLASTOMA CELL DIFFERENTIATION-RELATED PROTEIN. Length = 334	gi 3211975	685	1392	86	86	HTDAE52 HMEIS41 HIISAC93 HIISDH86 HDTAT56 HDTTFQ86 HTTPCQ24
192	784024							
193	784575							
194	785006							
195	785069							
196	785237							
197	786111							

198	787036	(AL008583) dJ327J16.1 (human ortholog of mouse outer arm Dynein light chain 4) [Homo sapiens] Length = 105	gnl PI D c1370730	123	518	100	100	ISSAL37
199	788991			74	556			HCLBI173
200	789125			3	515			ITXLS64
201	789626			98	742			HPBL42
202	789703			2	817			HDPJ62
203	789858			351	806			HATEH30
204	790848			891	1067			ITPDK53
205	790893			29	244			HPVE06
206	790912			293	544			HSET09
207	791386	ADP-ribosylation factor 1-directed GTPase activating protein [Rattus norvegicus] >sp Q62848 Q62848 ADP-RIBOSYLATION FACTOR 1-DIRECTED GTPASE: ACTIVATING PROTEIN. Length = 415	g l130494	1	366	73	84	DDQF129
208	791598			399	644			HOEDP59
209	791619			1	1698			HOGCS94
210	791628			125	466			HOEBP96
211	791751			3	464			HE80L02
212	792557	(AB004066) DEC1 [Homo sapiens] >pir C5547 C5547 basic helix-loop-helix factor DEC1 - human >sp O14503 O14503 DEC1. Length = 412	gnl PI D d1022575	231	470	92	93	HAMFQ15

213	792568	unknown [Saccharomyces cerevisiae] >pirS53571[S53571 hypothetical protein YIL128w - yeast (Saccharomyces cerevisiae) >sp P40469 MT18_YEAST DNA REPAIR/TRANSCRIPTION PROTEIN MET18/MMMS19. >gi 599989 unknown [Saccharomyces cerevisiae] {SUB 162- 1032} Length =	gi 763218	211	882	36	58	IIIVDIR47
214	792590	O-linked (GlcNAc transferase [Homo sapiens] >sp O15294 O15294 UDP-N- ACETYLGLUCOSAMINE--PEPTIDE N- ACETYLGLUCOSAMINYLTRANSFERASE SE 100 KD SUBUNIT (EC 2.4.1.-) (O- GLCNAC:TRANSFERASE P100 SUBUNIT). Length = 920	gi 2266994	1163	2656	100	100	HTTCQ93
215	793323	(AB008430) CDEP [Homo sapiens] >sp D1025178 D1025178 CDEP. Length = 1045	gnl P1D D1025178	3	1187	96	96	HIBWBJ67 HIBCIJ37 HAGER01 H2CBL95 HISBT02 HISBR20
216	793466							
217	793507							
218	793546							
219	793559							
220	793604							
221	794121	F46F6.1 (FRAGMENT). Length = 509	sp Q20473 Q20473	556	1089	43	67	HOEAN65 HFIAA16 HOEDV07
222	794295							
223	795241							
224	795286			132	1487			HTJNQ55 HHHBM95
225	795637							

226	796301	(AF053367) carboxyl terminal LIM domain protein [Mus musculus] >sp Q70400 Q70400 CARBOXYL TERMINAL LIM DOMAIN PROTEIN. Length = 326	gil2996196	142	1104	63	82	11KACQ38
227	796347			740	952			HOGCR67
228	796579	U2 small nuclear ribonucleoprotein B" [Homo sapiens] >pir A25910 A25910 small nuclear ribonucleoprotein (2B" - human Length = 225	gil340105	32	847	88	88	HOQAQ65
229	796590	(A1039700) antigen NY-CO-38 [Homo sapiens] >sp G3170200 G3170200 ANTIGEN NY-CO-38 >gil3170198 (AF039699) antigen NY-CO-37 [Homo sapiens] (SUB 1-403) Length = 652	gil3170200	54	572	41	65	HTXBD96
230	799783			1	198			HPNAA04
231	799784			1	282			HTPCY49
232	799785			176	373			HTPCW69
233	799786			26	397			HSEI18
234	799787			78	245			HTPDR86
235	799800			1	210			HTPDJ82
236	799808	pancreatic protease E precursor [Homo sapiens] >sp P09093 EL3A_HUMAN ELASTASE IIIA PRECURSOR (EC 3.4.21.70) (PROTEASE E). Length = 270	gil PID d1000660	2	820	97	97	HCCMD30

237	799977	(A1000342) DMBT1 protein, 5.8 kb transcript [Homo sapiens] >sp E328724 E328724 DMBT1 PROTEIN, 5.8 KB TRANSCRIPT PRECURSOR. Length = 1785	gnl PI D c328724	2	541	81	81	111PDX19
238	800149	(A1017365) frizzled-7 [Homo sapiens] >sp D1035649 D1035649 FRIZZLED-7. Length = 574	gnl PI D d1035649	3	188	96	96	111SIBC04
239	800189	NTGP4 [Nicotiana glauca] >sp G4097585 G4097585 NTGP4 (PRAGMATIC). Length = 344	gil 4097585	33	434	45	68	111DDQ25
240	800589	retinal-specific heterotrimeric GTP-binding protein beta subunit, G beta5L, [Mus musculus] >sp G1663629 G1663629 RETINAL-SPECIFIC HETEROTRIMERIC GTP-BINDING PROTEIN BETA SUBUNIT, G BETA5L. >gil 557738 guanine nucleotide regulatory protein [Mus musculus] {SU	gil 663629	137	1249	99	100	111ARAC68
241	800811	SH3-domain interacting protein [Homo sapiens] >sp Q15220 Q15220 PRPL-2 PROTEIN. >pir S52796 S52796 prpl.2 protein - human (fragment) {SUB 92-494; Length = 494	gnl PI D c1226443	2	601	100	100	111SKGN39
242	800857	p78 protein [Homo sapiens] >sp P20591 MX1_HUMAN INTERFERON-REGULATED RESISTANCE GTP-BINDING PROTEIN MXA (INTERFERON-INDUCED PROTEIN P78) (IFL-78K). {SUB 2-662; Length = 662	gil 190136	295	2274	96	96	111MTBX80
243	805721			3	224			111SKYW73
244	805818			143	994			111ABT11

245	806267	(AF022982) contains similarity to the A-type potassium current class of channel proteins [Caenorhabditis elegans] >sp O17001 O17001_123B12.6 PROTEIN. Length = 670	gi 2384910	2	1018	57	75	110TDM49
246	806579			971	1282			111ASC33
247	810625	(AF085691) multidrug resistance-associated protein 3A [Homo sapiens] >sp G4106442 G4106442 MULTIDRUG RESISTANCE-ASSOCIATED PROTEIN 3A. Length = 1238	gi 4106442	3	1019	96	96	111WFA006
248	811153	SHB=SRC HOMOLOG Y 2 PROTEIN. Length = 309	sp G545100 G545100	531	881	83	96	110QED71
249	811787			1201	1797			11EONN51
250	812314	ubiquitin-specific protease [Drosophila melanogaster] Length = 898	gn P11 c252797	648	1514	46	67	11USX071
251	812443	binding factor-2 box B [Drosophila melanogaster] >pir A42140 A42140 box B-binding factor-2 - fruit fly (Drosophila melanogaster) >sp P29747 BBF2_DROME:BOX B BINDING FACTOR-2 (BBF-2). Length = 515	gi 11064	2	733	67	85	11E8PW90
252	812498			1290	1550			11E8PW45
253	812504	(AF035737) general transcription factor 2-L; alternative splice product [Homo sapiens] >sp O43546 O43546 GENERAL TRANSCRIPTION FACTOR 2-L. ALTERNATIVE SPLICED PRODUCT. Length = 998	gi 2827180	3	1601	98	99	11E1AT66

254	813079	GS2NA [Homo sapiens] >pir JC252 JC2522 nuclear autoantigen - human Length = 713	gil805095	1	756	62	73	ICROB17
255	815889	centrin [Homo sapiens] >sp O15182 O15182 CENTRIN Length = 167	gnl P1D c314005	1	603	99	100	HOLEFN43
256	824358	oxysterol-binding protein [Homo sapiens] >pir A34581 A34581 oxysterol-binding protein - human >sp P22059 OXYB_HUMAN OXYSTEROL-BINDING PROTEIN. Length = 807	gil189403	415	1275	100	100	HMSK174
257	826144	ets-related protein [Homo sapiens] >gnl P1D c225719 erm [Homo sapiens] >pir S43692 S43692 transcription factor erm - human >sp P4116 IERM_HUMAN IETS- RELATED PROTEIN IERM (ETS TRANSLLOCATION VARIANT 5). Length = 510	gil479167	1	609	100	100	HNFJH73
258	826558	cholesterol esterase [Homo sapiens] >bbs I09185 pancreatic cholesterol esterase. CEase (internal fragment) (EC 3.1.1.13) [human, pWE 15, PTCF, Peptide Partial, 28 aa] [Homo sapiens] (SUB 458-485) Length = 747	gil180482	3 1	266 1077	96	96	HITAF67 HVANU76
260	827716	(AF008197) syncollin [Rattus norvegicus] >sp O35775 O35775 SYNCOL.LIN. >gil 3366638 (AF012887) sip9 [Rattus norvegicus] (SUB 8-145) Length = 145	gil2258437	2	403	72	84	HIVANR45
261	827722			1976	2116			HISCW21

262	827727	(AC002451) pyruvate dehydrogenase kinase isoform 4 [Homo sapiens] >gil1399197	1192	1557	100	100	115CC19
263	828238	pyruvate dehydrogenase kinase isoform 4 [Homo sapiens] >gil1399210 pyruvate dehydrogenase kinase isoform 4 [Homo sapiens] >sp Q16654 PDK4_HUMAN [PYRUVATE DEHYDROGENASE(LIPOAMIDE	2	301	100		HLTG039
264	828573	pancreatic zymogen granule membrane protein GP-2 [Homo sapiens]	3	1118			HGCAA50
265	828624	>pir G02091 G02091 pancreatic zymogen granule membrane protein GP-2 - human	1305	1520			HTOE164
266	828656	>sp P5259 GP2_HUMAN PANCREATIC SECRETORY GRANULE MEMBRANE MAJOR GLYCOPROTEIN GP2	185	403			HISD127
267	828848	PRECURSOR (PANCREATIC ZYMOGEN G1A	3	1220	97	97	HIVANS09
268	828929	casein kinase I alpha L [Rattus norvegicus] >sp P97634 P97634 CASEIN KINASE I ALPHA L >gil975691 casein kinase I-alpha [Mus musculus] [SUB 327-353] Length = 353	3	479	80	80	HMICG83
269	829008	GTP-binding protein [Homo sapiens] >sp Q43824 Q43824 GTP-BINDING PROTEIN Length = 442	17	694	80	81	HISA179

270	829086	small GTP-binding protein [Oryctolagus cuniculus] >pir A48500 A48500 small GTP-binding protein Rab25 - rabbit Length = 213	gi 436001	244	426	82	87	HTTDE66
271	829192	p1.K [Homo sapiens] Length = 603	gi 393017	455	1270	94	95	HTMEKC67
272	829310	SUP35 gene product [Xenopus laevis] >pir S58444 S58444 SUP35 protein - African clawed frog (fragment) Length = 614	gi 976219	3	527	90	95	HTAMFY36
273	829319	spermatid-specific [Mus musculus]		407	805			HTFDB42
274	829459	>pir A37363 A37363 histone H2B, testis - mouse (fragment) >sp Q64477 Q64477 HISTONE H2B (FRAGMENT). Length = 134	gi 556310	2	184	97	100	HTNFAA17
275	829527	(AL031532) yeast gtr2 homolog, novel small GTPase subfamily protein	gi 119429	489	806			HTTDP69
276	829736	[Schizosaccharomyces pombe] >sp O74544 O74544 YEAST GTR2 HOMOLOG, NOVEL, SMALL GTPASE SUBFAMILY PROTEIN. Length = 314	gi 119429	3	1049	69	86	HTGCM10
277	830552			329	1732			HTTEV24

278	830566	cathepsin E precursor [Homo sapiens] >gi181205 cathepsin E [Homo sapiens] >pirA42038/A34401 cathepsin E (EC 3.4.23.34) precursor - human >sp P14091 CATE_HUMAN CATHEPSIN E PRECURSOR (EC 3.4.23.34). >sp G40284 IG40284 CATHEPSIN E. CE=MATURE FORM (N-TERMI	gi181194	1	552	99	100	HTPRQ32
279	830568	tyrosine protein kinase [Homo sapiens] >sp Q08345 EDD1_HUMAN EPITHELIAL DISCOIDIN DOMAIN RECEPTOR 1 PRECURSOR (EC 2.7.1.12) (TYROSINE- PROTEIN KINASE; CAK) (CELL ADHESION KINASE) (TYROSINE KINASE; DDR) (DISCOIDIN RECEPTOR TYROSINE KINASE) (TRK E) (PROTEIN- T	gi1306475	3	1874	95	95	HTSGQ78
280	830569	lipase related protein 2 [Homo sapiens] >pir B43357 B43357 pancreatic lipase- related protein 2 - human >sp P54317 LIP2_HUMAN PANCREATIC LIPASE RELATED PROTEIN 2 PRECURSOR (EC 3.1.1.3). Length = 469	gi187232	3	1433	98	98	HSIAL52
281	830583	alpha-tropomyosin 5b [Rattus norvegicus] >pir D39816 D39816 tropomyosin 5b, fibroblast - rat >sp Q63609 Q63609 ALPHA-TROPOMYOSIN 5B Length = 248	gi207508	1	909	85	85	HAROA79

282	830613	clathrin-associated protein [Mus musculus] >pir S19693 S19693 AP47 protein - mouse >sp P33585 AP47 MOUSE CLATHRIN COAT ASSEMBLY PROTEIN AP47 (CLATHRIN COAT ASSOCIATED PROTEIN AP47) (GOLGI ADAPTOR AP-1 47 KD PROTEIN) (HA1 47 KD SUBUNIT) (CLATHRIN ASSEMBLY	gi 191986	3	1091	77	90	HE1TFJ47
283	830686			197	391			HSTAI126
284	830691			1343	1627			HSE071
285	830716	(AL031393) dJ733D15.1 (Zinc-finger protein) [Homo sapiens] Length = 496	gi 110121329909	3	713	62	74	HSE1F42
286	830792	kallikrein [Homo sapiens] >pir A24696 KQ110 tissue kallikrein (EC 3.4.21.35) precursor - human >sp P06870 KLK1_HUMAN GLANDULAR KALLIKREIN 1 PRECURSOR (EC 3.4.21.35) (TISSUE KALLIKREIN) (KIDNEY/PANCREAS/SALIVARY GLAND KALLIKREIN). >gi 386843 kallikrein [Hom	gi 186653	1	801	99	99	HSDSG96
287	830893			29	535			HPRTG34
288	830976	(AF077866) amino acid transporter E16 [Homo sapiens] >sp G3639058 G3639058 AMINO ACID TRANSPORTER E16. >gi 181908 E16 [Homo sapiens] {SUB 267- 507} Length = 507	gi 3639058	3	1244	53	73	HDPRH64

289	831043	adhesive protein - mussel (Trichomya hirsuta) (fragments) Length = 65	pir S42675 S42675	24	257	41	62	IIQAIH73
290	831131	pancreatic secretory trypsin inhibitor [Homo sapiens] >gi 190694 PST1 [Homo sapiens] >pir A27484 TIIUA pancreatic secretory trypsin inhibitor precursor - human >sp P00995 IPST_HUMAN PANCREATIC SECRETORY TRYPSIN INHIBITOR PRECURSOR (TUMOR-ASSOCIATED TRYPSI	gi 190688	23	301	86	86	IIMTIB28
291	831164			59	331			IIMSGI46
292	831173			194	475			IIMQIB05
293	831255	MLN 64 [Homo sapiens] >dh J038255_1 CAB1 [Homo sapiens] >pir 38027 38027 MLN 64 protein - human >sp Q14849 Q14849 MLN64 MRNA. Length = 445	gi 951279	198	431	85	92	IHSIU60
294	831327	reg gene homologue [Homo sapiens] >gi P1D d1004610 regenerating protein I beta [Homo sapiens] >gi P1D d1004643 regenerating protein I beta [Homo sapiens] >pir S34591 RGHU1B regenerating islet lectin I-beta precursor - human >sp P48304 LITB_HUMAN LITHOST	gi 487726	80	601	90	90	IIPASG51
295	831493	DARPP-32=DOPAMINE AND CAMP-REGULATED PHOSPHOPROTEIN. >gi 244402 DARPP-32 [Mus musculus] {SUB 1-27} Length = 204	sp G545790 G545790	2	256	97	97	IHSDF31

296	831500	endothelin-3 precursor [Homo sapiens] >pir A34378 A34378 endothelin-3 precursor - human >sp P14138 ET3_HUMAN ENDOTHELIN-3 PRECURSOR (ET-3). Length = 238	gi 182249	2	364	87	87	11WMEM06
297	831501			2	118			11SBO94
298	831502			339	527			11SCHI48
299	831508			160	354			11CRMN21
300	831509			450	752			11SCC33
301	831520			242	424			11HTLE36
302	831547	match: protein P30711 [Homo sapiens] Length = 240	gi 110103 c313869	2	766	91	92	11YTA02
303	831548	glutathione transferase T1 [Homo sapiens] >pir S44358 S44358 glutathione S- transferase Theta - human >sp P30711 GTT1_HUMAN GLUTATHIONE S-TRANSFERASE THETA 1 (EC 2.5.1.18) (CLASS-THETA). {SUB 2-240} Length = 240	gi 510905	3	257	97	97	11IGDQ55
304	831558			3	410			11IGCU20
305	831847			48	953			11TPE164
306	831893	(AF012023) integrin cytoplasmic domain associated protein: Icap-1a [Homo sapiens] >sp O14713 O14713 INTEGRIN CYTOPLASMIC DOMAIN ASSOCIATED PROTEIN. Length = 200	gi 2305238	167	589	78	78	11PJDB54
307	831903			881	1045			11DTEA17

308	831921	(AF013965) Zis [Rattus norvegicus] >gil2317754 (AF013966) Zis [Rattus norvegicus] >gil2317756 (AF013967) Zis [Rattus norvegicus] >sp O35986 O35986 Zis. Length = 332	gil2317752	66	410	70	78	IMUAR39
309	831923	(AF035527) EIF [Mus musculus] >sp O70273 O70273 ETS HOMOLOGOUS FACTOR (EIF) (EIF). Length = 300	gil3138930	133	1041	88	93	IIDQEG93
310	831959	cyclin-dependent kinase [Homo sapiens] >pir 68674 68674 cyclin-dependent kinase - human (fragment) >gil425143 cyclin-dependent kinase inhibitor [Homo sapiens] (SIB 18-181) Length = 181	gil986879	672	956	86	86	IIDPRV34 IIDPQA36
312	832107	T-cell receptor alpha enhancer-binding protein, long form - human Length = 399	pir A39625 A39625	2	244	91	91	IIDACF80 HCFI.R04
314	832146	CTP synthetase homolog [Mus musculus] >sp P70303 P70303 CTP SYNTHETASE HOMOLOG (CTPSH). Length = 586	gil1654186	3	587	69	77	IIEK0J09
315	832189	thymopoietin alpha [Homo sapiens] >pir A55741 A55741 thymopoietin alpha precursor - human Length = 694	gil508725	251	520	97	97	IISER65 HCUDS28
316	832295			3	617			

317	832334	coatmer [Bos taurus] >pir A49465 A49465 coatmer zeta chain - bovine >sp P35604 COPZ_BOVIN COATOMER ZETA SUBUNIT (ZETA-COAT PROTEIN) (ZETA-COP). Length = 177	gil441486	3	299	98	98	111IC179
318	832339	(AF049105) centrosomal Nek2-associated protein 1 [Homo sapiens] >sp O60588 O60588 CENTROSONAL NEK2-ASSOCIATED PROTEIN 1. Length = 2442	gil2984657	2	634	18	50	HE7TF56
319	832393	platelet-endothelial tetraspan antigen 3 [Homo sapiens] >sp P48509 C151_HUMAN PLATELET-ENDOTHELIAL TETRASPAN ANTIGEN 3 (PETA-3) (GP27) (MEMBRANE GLYCOPROTEIN SFA-1) (CD151 ANTIGEN). Length = 253	gil541613	49	591	81	81	11W111D38
320	832415	PC4 [Homo sapiens] >gil619161 PC4. p15 [Homo sapiens] >pir A54670 A54670 RNA polymerase II transcription cofactor p15 - human >sp P53999 P15_HUMAN ACTIVATED RNA POLYMERASE II TRANSCRIPTIONAL COACTIVATOR P15 (PC4) (P14). (SUB 2-127). Length = 127	gil531395	80	475	87	87	11C1DMB85
321	832422	(AF006751) ES/130 [Homo sapiens]		3	1112			11AMG1D22
322	832448	>sp O75300 O75300 ES/130. Length = 977	gil3299885	1	777	65	65	HAJBU71

323	832532	protein serine/threonine kinase [Homo sapiens] >pir A48082 A48082 mitogen-activated protein kinase p44-erk1 - human Length = 379	gij31221	2	532	100	100	100	11MKD/23
324	832621			1	462				112CIII76
325	832622	(AF056209) PAM COOH-terminal interactor protein 1 [Homo sapiens] >gij3560563 (AF056209) PAM COOH-terminal interactor protein 1 [Homo sapiens] >sp Q75901 Q75901 PAM COOH-TERMINAL INTERACTOR PROTEIN 1. Length = 435	gij3560563	78	569	97			112CAA56
326	835327			140	355				11TPCS09
327	835695	(AF031174) Ig-like membrane protein [Homo sapiens] Length = 1215	gij3766136	2	997	52		75	11DPIQ22
328	835857	(AC004549) TXBP151 [Homo sapiens] >sp Q60398 Q60398 TXBP151. Length = 563	gij3046307	1	1728	100		100	11EQI0228
329	836183			46	978				11WLGVI4
330	836190			1586	1813				11LTAV24
331	836196			2	319				11OECJ56
332	836253			1	363				11NSAC43
333	836372	Similar to sulfatase [Caenorhabditis elegans] >sp Q21376 Q21376 SIMILAR TO SULFATASE. NCBI GI: 1125842. Length = 705	gij1125842	794	1177	58		73	11OELR57
334	837077	similar to BPTI/KUNITZ inhibitor domain:	gnl P D c1345870	3	572	48		61	11EOMV66

335	837445	(AF046888) proliferation inducing ligand APRIL [Homo sapiens] >sp O75888 O75888 PROLIFERATION INDUCING LIGAND APRIL. Length = 250	gil3650492	801	1580	90	90	IIDQI1176
336	837620	(AF002210) copper chaperone for superoxide dismutase [Homo sapiens] >sp O14618 O14618 COPPER CHAPERONE FOR SUPEROXIDE DISMUTASE. Length = 274	gil2431868	1	930	99	99	IITLJDR72
337	837981	beta-1,6-N-acetylglucosaminyltransferase [Homo sapiens] >gil886273 beta-1,6-N- acetylglucosaminyltransferase [Homo sapiens] >pir A46293 A46293 beta-1,3- galactosyl-O-glycoprotein beta-1, 6-N-acetylglucosaminyltransferase (EC 2.4.1.102) - human >sp	gil183441	346	1740	58	74	IITPB003
338	837995	aminopeptidase N precursor (EC 3.4.11.2) [Homo sapiens] >pir A30325 A30325 membrane alanyl aminopeptidase (EC 3.4.11.2) precursor - human Length = 967	gil178536	301	3231	94	94	IIDP'AV72

339	838001	lysyl hydroxylase isoform 2 [Homo sapiens] >sp Q00469 PL02_HUMAN PROCOLLAGEN-LYSINE-2- OXOGLUTARATE 5-DIOXYGENASE 2 PRECURSOR (EC 1.14.11.4) (LYSYL HYDROXYLASE 2) (LH2). Length = 737	gi 2138314	1	2553	93	93	110HAU14
340	838237	alpha-N-acetylgalactosaminide alpha-2,6- sialyltransferase [Gallus gallus] >pir A49880 A49880 alpha-N- acetylgalactosaminide alpha-2,6- sialyltransferase (EC 2.4.99.3) - chicken >sp Q92183 CAG3_CHICK ALPHA-N- ACETYL GALACTOSAMINIDE ALPHA- 2,6-SIALYLTRANSFERASE	gi 453197	3	416	58	74	11WMFG72
341	838700	(AL032653) similar to Ubiquitin- conjugating enzymes: (AF027302) TNF-alpha stimulated ABC protein [Homo sapiens] >sp O14897 O14897 TNF-ALPHA STIMULATED ABC PROTEIN. Length = 807	gn P D c 1350657	2	1756	61	78	11DTGB81 HAMGK18
342	838805			3	485			
343	839096			666	1559	84	84	11DJPJC76
344	839185	similar to ATP-binding transport protein family (ABC transporters) [Caenorhabditis elegans] >sp Q20306 Q20306 GCN20 PROTEIN HOMOLOG. Length = 712	gi 500734	1323	2165	49	69	11DPFR49
345	839588			710	904			11LJHEV35

346	839589	synthetic preproinsulin [artificial sequence] >gi158103 reading frame proinsulin [unidentified] {SUB 28-114} >gi208664 insulin B chain [artificial sequence] {SUB 28-58} >gi208660 insulin beta chain [artificial sequence] {SUB 29-58} >gi929915 insulin C	gi208668	1	498	80	80	IICCM104
347	839733	RG1.2 [Homo sapiens] >sp O15211 O15211 RGL2 >gnl PID d1037179 (AB012295) GDS-related protein [Homo sapiens] {SUB 656-777} Length = 777	gnl PID d1186796	1098	2681	90	90	IIVAC102
348	839874	mitochondrial NAD(P)+ -dependent malic enzyme [Homo sapiens] >pir A39503 A39503 malate dehydrogenase (NAD+) (EC 1.1.1.-) precursor. mitochondrial - human >sp P23368 MAOM_HUMAN MALATE OXIDOREDUCTASE [NAD]. MITOCHONDRIAL PRECURSOR (EC 1.1.1.40) (MALIC ENZYME	gi187300	102	1058	96	97	IIDPT941
349	840017	FKBP65 binding protein [Mus musculus] >pir I49669 I49669 FKBP65 binding protein - mouse >sp Q61576 Q61576 FK506 BINDING PROTEIN 6 (65 KDA) (FKBP65 BINDING PROTEIN). Length = 581	gi1894162	2	1303	86	92	IIL1B167
350	840124	P24 protein [Mus musculus]		937	1311			IIN1GX94
351	840222	>sp P97799 p97799 VESICULAR MEMBRANE PROTEIN P24 (P24 PROTEIN). Length = 196	gnl PID d1019688	28	747	35	47	IISES36

352	840617	(AF033861) type III adenylyl cyclase [Homo sapiens] >sp G4104226 G4104226 TYPE III ADENYLYL CYCLASE; >gnl PID d1026367 (AB011083) KIAA0511 protein [Homo sapiens] {SUB 212-1144} >sp G299652 G299652 TYPE III ADENYLYL CYCLASE; TYPE III AC {EC 4.6.1.1}; {SUB	g4104226	35	2599	91	91	11TTPDM11
353	840641	RGS10 protein - human Length = 173	pir S71812 S71812	2	622	100	100	11ULFJ24
354	840792	sigma 3A protein [Homo sapiens] >gi 1923270 AP-3 complex sigma3A subunit [Homo sapiens] >gnl PID d1010444 clathrin coat assembly protein-like [Homo sapiens] >gi 3462900 (AF084575) adaptor protein complex-3 sigma3A subunit isoform [Mus musculus] >gi 192327	gnl PID c256812	1	699	100	100	11OJET19
355	840915	Tob [Homo sapiens] Length = 345	gnl PID d1008002	411	1469	82	82	112MBF94
356	841059			583	828			110SBI50
357	841325	FAC1 gene product [Homo sapiens] >pir G01252 G01252 small GTP binding protein, homologous to SEC4 - human >sp Q12830 Q12830 FETAL ALZ-50-REACTIVE CLONE 1 (FAC1). Length = 810	gnl 276428	6	989	95	95	11FEBE52
358	841713			3	872			11WHGW75
359	842324			487	837			11LWBQ31
360	842386			201	671			11CFDA62

361	842454	mitochondrial ATPase inhibitor [Rattus norvegicus] >gnl p D d1002924 ATPase inhibitor protein precursor [Rattus sp.] >pir S0738 S0738 ATPase inhibitor protein precursor, mitochondrial - rat >sp Q03344 A1P_RAT ATPASE INHIBITOR, MITOCHONDRIAL PRECURSOR.	gi 517226	1	231	76	88	IIVAMF27
362	842768	d1434P1.3 [Homo sapiens] >gi 1592565 DEAD-box protein p72 [Homo sapiens]		179	400			IIRABQ15
363	842999	>pir S72367 S72367 ATP-dependent RNA helicase - human >sp Q92841 P72_HUMAN PROBABLE RNA-DEPENDENT HELICASE: P72 (DEAD-BOX PROTEIN P72). Length = 650	gnl P D c1249592	2	1354			IINTSM88
364	843830			3	635	93	93	IIMSP189
365	844723	(AF092557) LIM domain only 7 [Homo sapiens] >sp Q4028544 G4028544 LIM DOMAIN ONLY 7 (FRAGMENT). Length = 120	gi 4028544	1	66			IILYBO68
366	844868			1	1179	56	74	IHIPIBC57
367	845258	MRAS2 gene product [Rhizomucor racemosus] Length = 198	gi 553070	131	925	30	45	IIRAKW86
368	845373	(AB003184) ISLR [Homo sapiens]		183	1847			IINTEE61
369	845412	>sp O14498 O14498 ISLR PRECURSOR. Length = 428	dbj AB003184_1	303	1178	87	87	IICRNP15
370	IHSFD43R			29	283			IHSFD43

371	IIQSEQ76R		165	308	IIQSEQ76
372	IIISDS43R		1	141	IIISDS43
373	IIPIJY28R		53	136	IIPIJY28
374	IIIPBW71R		29	94	IIIPBW71
375	IIQAG14R		18	173	IIQAG14
376	IIVANP48R		14	271	IIVANP48
377	IIIGBG086R	(AB005546) porcine serum amyloid P component (SAP) [Sus scrofa] >sp O19063 O19063 PORCINE SERUM AMYLOID P COMPONENT (SAP) PRECURSOR (SAP). Length = 224	2	139	IIIGBG086
378	IIISDW59R	(AB012223) ORF2 [Canis familiaris] >sp O62658 O62658 LINE-1 ELEMENT ORF2. Length = 1275	261	647	IIISDW59
379	IIDBAN116R	(AF000381) non-functional folate binding protein [Homo sapiens] >sp O14597 O14597 NON-FUNCTIONAL FOLATE BINDING PROTEIN. Length = 254	189	416	IIDBAN116
380	IIITPGD92R	(AF016692) small intestinal mucin MUC3 [Homo sapiens] >pir PC4395 PC4395 mucin 3 - human (fragment) >sp O14760 O14760 SMALL INTESTINAL MUCIN MUC3 (FRAGMENT). Length = 648	3	308	IIITPGD92

381	IIHFLB69R	(AF018432) dUTPase [Homo sapiens] >gil144332 deoxyuridine nucleotidohydrolase [Homo sapiens] >gil1421818 deoxyuridine triphosphatase [Homo sapiens] >pir(G02777[G02777 dUTP pyrophosphatase (EC 3.6.1.23) - human >gil292877 dUTP nucleotidohydrolase [Homo sa	3	245	100	100	IIHFLB69
382	IIPDEH50R	(AF026689) prostate-specific transglutaminase [Homo sapiens] >sp O75320 O75320 PROSTATE- SPECIFIC TRANSGLUTAMINASE (FRAGMENT). Length = 51	2	166	66	72	IIPDEH50
383	IIMTMA16R	(AF042081) SH3 domain binding glutamic acid-rich-like protein [Homo sapiens] >sp O75368 O75368 SH3 DOMAIN BINDING GLUTAMIC ACID-RICH-LIKE PROTEIN. Length = 114	3	299	100	100	IIMTMA16
384	IITNAI171R	(AF080484) thyroglobulin [Homo sapiens] >sp G341505 G3415051 THYROGLOBULIN (FRAGMENT). Length = 680	2	199	95	95	IITNAI171
385	IITPGI.88R	(AF081673) bile salt-dependent lipase oncofetal isoform [Homo sapiens] >sp O75612 O75612 BILE SALT- DEPENDENT LIPASE: ONCOFETAL ISOFORM (FRAGMENT). Length = 612	3	434	97	98	IITPGI.88

386	IIMCIA86R	actin [Absidia glauca] >pir[S03109]S03109 actin - pin mould (Absidia glauca) (fragment) >sp P10982 ACT1_ABSGL ACTIN 1 (FRAGMENT). >gil669036 actin [Absidia glauca] {SUB 3-140} Length = 140	gil578097	2	250	88	100	IIMCIA86
387	IIAPOC60R	alpha-catenin [Homo sapiens] >gil4092761 (AF102803) alphaE-catenin [Homo sapiens] >pir JN0607 JN0607 alpha-catenin - human >sp P3522 CTN1_HUMAN ALPHA-1 CATENIN (CADHERIN-ASSOCIATED PROTEIN) (ALPHA E-CATENIN). Length = 906	gnl P1D Q1003485	2	505	77	80	IIAPOC60
388	IIDTFE89R	antibody, heavy chain variable region to IIIV1 gp120 [Homo sapiens] Length = 127	gil732750	3	329	75	78	IIDTFE89
389	IIAJBO38R	Bat2 [Homo sapiens] >pir S3767 S37671 bat2 protein - human Length = 1870	gil29375	1	435	94	94	IIAJBO38
390	IICCMAN90R	BILE SALT-DEPENDENT LIPASE. Length = 720	sp Q16398 Q16398	3	329	75	75	IICCMAN90
391	IITLIIH34R	camitine O-acetyltransferase (EC 2.3.1.7) precursor, mitochondrial - human >sp P43155 CACP_HUMAN CARNITINE: O-ACETYLTRANSFERASE (EC 2.3.1.7) (CARNITINE ACETYLASE) (CAT) (FRAGMENT). {SUB 3-626} Length = 626	pir A55720 A55720	3	602	97	97	IITLIIH34

392	IIWIIIPY22R	CLN3 protein [Homo sapiens] >gnl P1Dc283670 CLN3 protein [Homo sapiens] >gil2947055 (AC002425) CLN3 [Homo sapiens] >gil3337387 (AC002544) CLN [Homo sapiens] >gil4102729 (AF015593) CLN3 protein [Homo sapiens] >pir A57219/A57219 Batten disease-related prot	gil1039423	1	432	95	95	IIWIIIPY22
393	IICWFF39R	collagen alpha 1(V) chain precursor [Homo sapiens] >sp P20908 CA15_HUMAN PROCOLLAGEN ALPHA 1(V) CHAIN PRECURSOR. >gil1020326 alpha-1 type V collagen [Homo sapiens] {SUB 1-36} Length = 1838	gnl P1Djd1015029	3	407	65	65	IICWFF39
394	IIIBHBA92R	cytochrome oxidase subunit I [Homo sapiens] >sp P50656 COXI_HUMAN CYTOCHROME C OXIDASE POLYPEPTIDE 1 (EC 1.9.3.1) (FRAGMENT). Length = 102	gil348683	31	240	41	58	IIIBHBA92
395	IIITLIIP03R	dipeptidase precursor [Homo sapiens] Length = 411	gnl P1Djd1002931	3	413	92	92	IIITLIIP03
396	IICCMAA63R	elastase III B [Homo sapiens] >pir B29934 B29934 pancreatic elastase (EC 3.4.21.36) IIB precursor - human >sp P08861 HEL3B_HUMAN ELASTASE IIB PRECURSOR (EC 3.4.21.70) (PROTEINASE E). Length = 270	gil182035	1	252	96	96	IICCMAA63

397	HE8EZ78R	endosomal protein [Homo sapiens] >pir[S44243]S44243 endosomal protein - human >sp[Q15075]Q15075 ENDOSOMAL PROTEIN. Length = 1411	gi 475934	2	352	98	100	HE8EZ78
398	HG1AQ29R	erythroid DNA-binding protein [Homo sapiens] >gi 31243 Eryf1 transcription factor (AA 1-413) [Homo sapiens] >pir[A34888]A34888 transcription factor GATA-1 - human >sp P15976 GAT1_HUMAN ERYTHROID TRANSCRIPTION FACTOR (GATA-1) (ERYF1) (GF-1) (NF-E1). Length	gi 183072	1	186	50	54	HG1AQ29
399	HA1SD82R	fibrinogen gamma-prime chain [Homo sapiens] >sp P04469 FIBH_HUMAN FIBRINOGEN GAMMA-B CHAIN PRCUCRSOR (FIBRINOGEN GAMMA'). >gi 182443 gamma fibrinogen type B (AA at 202) [Homo sapiens] [SUB 285-453]; Length = 453	gi 182440	1	399	98	100	HA1SD82
400	I12LAS44R	gamma subunit of CCT chaperonin [Homo sapiens] >pir[S61529]A38983 TCP1 ring complex protein TRiC5 - human Length = 544	gi 671527	75	560	99	99	I12LAS44
401	HTXPA42R	GTP-binding protein (rab7) [Canis familiaris] >pir B30413 B30413 GTP-binding protein rab7 - dog Length = 207	gi 164058	166	432	98	100	HTXPA42

402	IIHWAI157R	hCRMP-2 [Homo sapiens] >gil1244400 related protein-2 [Homo sapiens] >gil2967519 N2A3 [Homo sapiens] >pir1C5317/C5317 dihydropyrimidinase- related protein 2 - human >sp16555IDPY2_HUMAN DIHYDROPYRIMIDINASE RELATED PROTEIN-2 (DRP)	2	121	92	94	IIHWAI157
403	IIAIEJ39R	HSJ1a [Homo sapiens] >pirS23509/S23509 dnaJ protein homolog - human Length = 277	2	370	84	84	IIAIEJ39
404	IIOEMQ04R	hypoxia-inducible factor 1 alpha [Homo sapiens] >gil144013 ARNT interacting protein [Homo sapiens] >pir138972/138972 hypoxia-inducible factor 1 alpha - human >sp16665/HIF1A_HUMAN HYPOXIA- INDUCIBLE FACTOR 1 ALPHA (HIF-1 ALPHA) (ARNT INTERACTING PROTEIN)	3	299	100	100	IIOEMQ04
405	IIAPBR18R	Ig kappa L-chain variable region [Homo sapiens] Length = 122	29	325	67	70	IIAPBR18
406	IIOENU56R	L-arginine: glycine amidinotransferase [Homo sapiens] >pirS4161/S4161 L-	1	288			IIOENU56
407	IIAGGB37R	arginine--glycine amidinotransferase - human Length = 391	2	238	83	83	IIAGGB37

408	HCCMC02R	lipase related protein 2 [Homo sapiens] >pir B43357 B43357 pancreatic lipase-related protein 2 - human >sp P54317 P2_HUMAN PANCREATIC LIPASE RELATED PROTEIN 2 PRECURSOR (EC 3.1.1.3). Length = 469	gi 187232	1	357	61	64	HCCMC02
409	HAHDO57R	located at OATL1 [Homo sapiens] >sp Q14827 Q14827 DNA SEGMENT, JOHNS HOPKINS UNIVERSITY 1 (MG21) (FRAGMENT). Length = 166	gi 950411	3	536	100	100	HAHDO57
410	HOEMK29R	lysyl oxidase-2 [Mus musculus] >sp P97873 P97873 LYSYL OXIDASE-LIKE (LYSYL OXIDASE-2) (LYSYL OXIDASE-LIKE PROTEIN) (FRAGMENT). Length = 110	gi 2636697	3	116	97	97	HOEMK29
411	HRADJ65R	ORF protein; C-terminal (aa 125-319; 196aa) [Homo sapiens] Length = 196	gi 37610	1	357	98	98	HRADJ65
412	HTPCT95R	pancreatic elastase IIB zymogen [Homo sapiens] >pir C26823 C26823 pancreatic elastase II (EC 3.4.21.71) B precursor - human >sp P08218 P08218_HUMAN ELASTASE 2B PRECURSOR (EC 3.4.21.71). Length = 269	gi 182060	2	340	98	98	HTPCT95
413	HLQFY56R	pancreatitis associated protein [Homo sapiens] Length = 174	gi 189601	281	493	94	94	HLQFY56

414	IICCMD33R	phospholipase [Homo sapiens] >gi387025 phospholipase [Homo sapiens] >gi2769697 (AC003982) Phosphatidylcholine 2- acyldolase [Homo sapiens] >pirC25793[P/S/H] phospholipase A2 (EC 3.1.1.4) precursor, pancreatic - human >sp P04054 PA21_HUMAN PHOSPHOLIPASE	gi1190013	109	345	77	77	IICCMD33
415	IIDPAQ04R	PQ-rich protein [Homo sapiens] >pirS58222[S58222 PQ-rich protein - human >sp Q15184 Q15184 PQ-RICH PROTEIN. Length = 400	gi929660	3	125	85	85	IIDPAQ04
416	IICF41.96R	PRSM1 [Homo sapiens] >pirJC4963]JC4963 metalloproteinase 1 (EC 3.4.24.-) - human >sp Q15779 Q15779 PRSM1. Length = 318	gi1354931	3	194	89	89	IICF41.96
417	IITPGL86R	putative surface glycoprotein [Homo sapiens] >sp P53801 C211_HUMAN PUTATIVE SURFACE GLYCOPROTEIN C21ORF1 PRECURSOR (C21ORF3). Length = 180	gn P1D c188111	32	322	85	85	IITPGL86

418	III.QGB61R	reg gene homologue [Homo sapiens] >gnl PI D 1004610 regenerating protein 1 beta [Homo sapiens] >gnl PI D 1004643 regenerating protein 1 beta [Homo sapiens] >pir S34591 RGHUB regenerating islet lectin 1-beta precursor - human >sp P48304 ITB_HUMAN ITTHOST	21	182	92	92	III.QGB61
419	IIWDAK95R	RNA splicing-related protein [Rattus norvegicus] >sp O54729 O54729 BRAIN. Length = 712	141	362	82	88	IIWDAK95
420	IIIE9DG72R	selenium-binding protein [Homo sapiens] >pir G01872 G01872 selenium-binding protein - human >sp Q13228 Q13228 SELENIUM-BINDING PROTEIN. Length = 472	1	414	95	96	IIIE9DG72
421	IIDPOY89R	Similar to sulfatase [Caenorhabditis elegans] >sp Q21376 Q21376 SIMILAR TO SULFATASE. NCBI GI: 1125842. Length = 709	132	452	47	71	IIDPOY89
422	IIAHEJ13R	sperm membrane protein [Rattus norvegicus] >pir A35981 A35981 sperm membrane protein - rat Length = 191	1	366	58	60	IIAHEJ13
423	IIOEMR16R	tyrosine phosphatase precursor [Homo sapiens] >sp Q14513 Q14513 TYROSINE PHOSPHATASE PRECURSOR (EC 3.1.3.48). Length = 793	3	80	76	84	IIOEMR16
424	IIICFCM83R	ubiquitin--protein ligase E1 homolog - human Length = 1058	168	269	94	94	IIICFCM83
425	II6BSB07R		1	105			II6BSB07

426	IIAGCC01R	1	219	IIAGCC01
427	IIAQAM88R	49	372	IIAQAM88
428	IIAUBA62R	3	233	IIAUBA62
429	IIICMA07R	3	164	IIICMA07
430	IIIRGUA45R	132	293	IIIRGUA45
431	IIIBJHW09R	142	309	IIIBJHW09
432	IIIMBJ92R	3	173	IIIMBJ92
433	IIICGRC37R	1	219	IIICGRC37
434	IIICROI22R	105	236	IIICROI22
435	IIDTLK21R	184	351	IIDTLK21
436	IIDTLX11R	234	518	IIDTLX11
437	IIIC2CM25R	27	470	IIIC2CM25
438	IIIE9F119R	1	183	IIIE9F119
439	IIIEGAD29R	234	344	IIIEGAD29
440	IIIFKHC10R	118	267	IIIFKHC10
441	IIIFPAE25R	174	332	IIIFPAE25
442	IIIGBHA95R	3	161	IIIGBHA95
443	IIIBEA82R	139	387	IIIBEA82
444	IIISCX64R	1	312	IIISCX64
445	IIICAB30R	1	72	IIICAB30
446	IIILDOW24R	147	296	IIILDOW24
447	IIILBA89R	56	220	IIILBA89
448	IIILQDE48R	299	523	IIILQDE48
449	IIINED154R	1	84	IIINED154
450	IIINIGQ70R	1	423	IIINIGQ70
451	IIOSMV19R	151	291	IIOSMV19
452	IIIPGJ41R	89	340	IIIPGJ41
453	IIITTD11R	1	90	IIITTD11
454	IIULEB88R	2	376	IIULEB88
455	IIUSJN92R	284	460	IIUSJN92
456	IIWAEJ52R	1	285	IIWAEJ52
457	IIWLM512R	136	321	IIWLM512

458	IIWL.WG58R	X104 [Homo sapiens] >pir 54378 54378	1	108			IIWL.WG58
459	IIAIDL46R	gene X104 protein - human >sp Q15883 Q15883 X104. >gi 3462868 (AF083892) tight junction protein ZO-2 isoform A [Homo sapiens] {SUB 1-166} >gi 3462870 (AF083893) tight junction protein ZO-2 isoform C [Homo sapiens] {S	3	224	55	57	IIAIDL46
			gi 498013				

The first column of Table 1 shows the "SEQ ID NO:" for each of the 459 pancreatic cancer antigen polynucleotide sequences of the invention.

The second column in Table 1, provides a unique "Sequence/Contig ID" identification for each pancreas and/or pancreatic cancer associated sequence. The third column in Table 1, "Gene Name," provides a putative identification of the gene based on the sequence similarity of its translation product to an amino acid sequence found in a publicly accessible gene database, such as GenBank (NCBI). The great majority of the cDNA sequences reported in Table 1 are unrelated to any sequences previously described in the literature. The fourth column, in Table 1, "Overlap," provides the database accession no. for the database sequence having similarity. The fifth and sixth columns in Table 1 provide the location (nucleotide position nos. within the contig), "Start" and "End", in the polynucleotide sequence "SEQ ID NO:X" that delineate the preferred ORF shown in the sequence listing as SEQ ID NO:Y. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the portion of SEQ ID NO:X delineated by the nucleotide position nos. "Start" and "End". Also provided are polynucleotides encoding such proteins and the complementary strand thereto. The seventh and eighth columns provide the "% Identity" (percent identity) and "% Similarity" (percent similarity) observed between the aligned sequence segments of the translation product of SEQ ID NO:X and the database sequence.

The ninth column of Table 1 provides a unique "Clone ID" for a clone related to each contig sequence. This clone ID references the cDNA clone which contains at least the 5' most sequence of the assembled contig and at least a portion of SEQ ID NO:X was determined by directly sequencing the referenced clone. The reference clone may have more sequence than described in the sequence listing or the clone may have less. In the vast majority of cases, however, the clone is believed to encode a full-length polypeptide. In the case where a clone is not full-length, a full-length cDNA can be obtained by methods described elsewhere herein.

Table 3 indicates public ESTs, of which at least one, two, three, four, five, ten, or more of any one or more of these public ESTs are optionally excluded from the invention.

SEQ ID NO:X (where X may be any of the polynucleotide sequences disclosed in the sequence listing as SEQ ID NO:1 through SEQ ID NO:459) and the translated SEQ ID NO:Y (where Y may be any of the polypeptide sequences disclosed in the sequence listing as SEQ ID NO:460 through SEQ ID NO:918) are sufficiently accurate and otherwise suitable for a

variety of uses well known in the art and described further below. For instance, SEQ ID NO:X has uses including, but not limited to, in designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the related cDNA clone contained in a library deposited with the ATCC. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y have uses that include, but are not limited to, generating antibodies which bind specifically to the pancreatic cancer antigen polypeptides, or fragments thereof, and/or to the pancreatic cancer antigen polypeptides encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing the related cDNA clone (deposited with the ATCC, as set forth in Table 1). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO:X.

The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to vectors or plasmids which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC on:

5 **Table 2**

ATCC Deposits	Deposit Date	ATCC Designation Number
LP01, LP02, LP03, LP04, LP05, LP06, LP07, LP08, LP09, LP10, LP11,	May-20-97	209059, 209060, 209061, 209062, 209063, 209064, 209065, 209066, 209067, 209068, 209069
LP12	Jan-12-98	209579
LP13	Jan-12-98	209578
LP14	Jul-16-98	203067
LP15	Jul-16-98	203068
LP16	Feb-1-99	203609
LP17	Feb-1-99	203610
LP20	Nov-17-98	203485
LP21	Jun-18-99	PTA-252
LP22	Jun-18-99	PTA-253
LP23	Dec-22-99	PTA-1081

each is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as shown in Table 5. These deposits are referred to as "the deposits" herein. The tissues from which the clones were derived are listed in Table 5, and the vector in which the cDNA is contained is also indicated in Table 5. The deposited material includes the cDNA clones which were partially sequenced and are related to the SEQ ID NO:X described in Table 1 (column 9). Thus, a clone which is isolatable from the ATCC Deposits by use of a sequence listed as SEQ ID NO:X may include the entire coding region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene. Although the sequence listing lists only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to complete the sequence of the DNA included in a clone isolatable from the

ATCC Deposits by use of a sequence (or portion thereof) listed in Table 1 by procedures hereinafter further described, and others apparent to those skilled in the art.

Also provided in Table 5 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res.* 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., *Nucleic Acids Res.* 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., *Strategies* 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into *E. coli* strain XL-1 Blue, also available from Stratagene.

Vectors pSport1, pCMVSPORT 1.0, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus* 15:59 (1993). Vector lafmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: (1991).

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the cDNA contained in a deposited cDNA clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include, but are not limited to, preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the cDNA contained in the related cDNA clone in the deposit, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or the related cDNA clone (See, e.g., columns 1 and 9 of Table 1). The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in a deposited library. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, and/or a polypeptide encoded by the the dDNA in the related cDNA clone contained in a deposited library, are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the complement of the coding strand of the related cDNA clone contained in a deposited library.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence would unduly burden the disclosure of this application. Accordingly, for each "Contig Id" listed in the first column of Table 3, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described in the second column of Table 3 by the general formula of a-b, each of which are uniquely defined for the SEQ ID NO:X corresponding to that Contig Id in Table 1. Additionally, specific embodiments are directed to polynucleotide sequences excluding at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. for each Contig Id which may be

included in column 3 of Table 3. In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example.

Table 3.

Sequence/ Contig ID	General formula	Genbank Accession No.
456379	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 551 of SEQ ID NO:1, b is an integer of 15 to 565, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:1, and where b is greater than or equal to a + 14.	R34554, AA018972, AA055489
462108	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1677 of SEQ ID NO:2, b is an integer of 15 to 1691, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:2, and where b is greater than or equal to a + 14.	T79903, R46289, R73001, R73606, N30140, N35752, W32520, W32636, AA018675, AA018676, AA040600, AA040683, AA070495, AA070381, AA083072, AA134451, AA207060, AA207086
503446	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 466 of SEQ ID NO:3, b is an integer of 15 to 480, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:3, and where b is greater than or equal to a + 14.	
507841	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 594 of SEQ ID NO:4, b is an integer of 15 to 608, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:4, and where b is greater than or equal to a + 14.	R12126, R14285
509287	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 682 of SEQ ID NO:5, b is an integer of 15 to 696, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:5, and where b is greater than or equal to a + 14.	H01699, H94037, N30572, N57219, N64393, N92189, AA035664, AA037022, AA045335, AA045422, AA056367, AA115587
509672	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 278 of SEQ ID NO:6, b is an integer of 15 to 292, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:6, and where b is greater than or equal to a + 14.	
509673	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 348 of SEQ ID NO:7, b is an integer of 15 to 362, where both a and	

	b correspond to the positions of nucleotide residues shown in SEQ ID NO:7, and where b is greater than or equal to a + 14.	
518767	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 391 of SEQ ID NO:8, b is an integer of 15 to 405, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:8, and where b is greater than or equal to a + 14.	
522008	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1013 of SEQ ID NO:9, b is an integer of 15 to 1027, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:9, and where b is greater than or equal to a + 14.	T63280, R50010, R78743, R78742, H52248, H52346, H91191, AA028894, AA031289, AA121197, AA150816, AA160833
524112	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1501 of SEQ ID NO:10, b is an integer of 15 to 1515, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:10, and where b is greater than or equal to a + 14.	H49520, H66748, H68803, H68904, N45520, W42600, W42573, AA134942, AA151361, AA227110, AA251434
525971	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 833 of SEQ ID NO:11, b is an integer of 15 to 847, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:11, and where b is greater than or equal to a + 14.	W81027, AA133066
527156	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 492 of SEQ ID NO:12, b is an integer of 15 to 506, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:12, and where b is greater than or equal to a + 14.	W23806
532502	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 253 of SEQ ID NO:13, b is an integer of 15 to 267, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:13, and where b is greater than or equal to a + 14.	
533459	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 905 of SEQ ID NO:14, b is an integer of 15 to 919, where both a and b correspond to the positions of nucleotide residues	

	shown in SEQ ID NO:14, and where b is greater than or equal to $a + 14$.	
533551	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2545 of SEQ ID NO:15, b is an integer of 15 to 2559, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:15, and where b is greater than or equal to $a + 14$.	H44763, H44764, AA011378, AA011366, AA215758
537850	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1490 of SEQ ID NO:16, b is an integer of 15 to 1504, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:16, and where b is greater than or equal to $a + 14$.	T68458, T68523, T83911, R07511, R07564, R10442, R11516, T80802, T81206, T83580, T83740, T85796, R06434, R06489, H40512, H47544, H47543, R85697, R89315, R89396, R91325, R96709, H59265, H59311, H64291, H78244, H78445, H90091, H94341, H94427
537925	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 819 of SEQ ID NO:17, b is an integer of 15 to 833, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:17, and where b is greater than or equal to $a + 14$.	AA085845
538160	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 629 of SEQ ID NO:18, b is an integer of 15 to 643, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:18, and where b is greater than or equal to $a + 14$.	W52418
540420	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 326 of SEQ ID NO:19, b is an integer of 15 to 340, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:19, and where b is greater than or equal to $a + 14$.	
540802	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 659 of SEQ ID NO:20, b is an integer of 15 to 673, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:20, and where b is greater than or equal to $a + 14$.	R27496, W05560, W40286, AA147911
540989	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 401 of SEQ ID NO:21, b is an integer of 15 to 415, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:21, and where b is greater than	

	or equal to $a + 14$.	
540997	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 619 of SEQ ID NO:22, b is an integer of 15 to 633, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:22, and where b is greater than or equal to $a + 14$.	W39752
548735	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2409 of SEQ ID NO:23, b is an integer of 15 to 2423, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:23, and where b is greater than or equal to $a + 14$.	T61438, R72243, AA134330
549709	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 370 of SEQ ID NO:24, b is an integer of 15 to 384, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:24, and where b is greater than or equal to $a + 14$.	
550007	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 886 of SEQ ID NO:25, b is an integer of 15 to 900, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:25, and where b is greater than or equal to $a + 14$.	AA058407
550118	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1308 of SEQ ID NO:26, b is an integer of 15 to 1322, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:26, and where b is greater than or equal to $a + 14$.	
550148	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 443 of SEQ ID NO:27, b is an integer of 15 to 457, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:27, and where b is greater than or equal to $a + 14$.	
550870	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 582 of SEQ ID NO:28, b is an integer of 15 to 596, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:28, and where b is greater than or equal to $a + 14$.	

552506	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 422 of SEQ ID NO:29, b is an integer of 15 to 436, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:29, and where b is greater than or equal to a + 14.	
553765	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1300 of SEQ ID NO:30, b is an integer of 15 to 1314, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:30, and where b is greater than or equal to a + 14.	T56196, T60502, T68045, T68126, T68223, T68924, T68956, T69698, T70509, T71155, T72771, T73042, T74806, H47199, H93928
554050	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1453 of SEQ ID NO:31, b is an integer of 15 to 1467, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:31, and where b is greater than or equal to a + 14.	T47267, T71354, R60150, R73621, H61209, H61252, H61301, H62114, W73095, AA100106
554186	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2332 of SEQ ID NO:32, b is an integer of 15 to 2346, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:32, and where b is greater than or equal to a + 14.	
554716	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 445 of SEQ ID NO:33, b is an integer of 15 to 459, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:33, and where b is greater than or equal to a + 14.	AA155695
556791	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 615 of SEQ ID NO:34, b is an integer of 15 to 629, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:34, and where b is greater than or equal to a + 14.	
557121	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 904 of SEQ ID NO:35, b is an integer of 15 to 918, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:35, and where b is greater than or equal to a + 14.	R64392, N79271, N93935, W40435, W94836, AA032255, AA033626, AA043229, AA043230, AA150687, AA150859
557199	Preferably excluded from the present invention are	

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 788 of SEQ ID NO:36, b is an integer of 15 to 802, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:36, and where b is greater than or equal to a + 14.	
557293	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2079 of SEQ ID NO:37, b is an integer of 15 to 2093, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:37, and where b is greater than or equal to a + 14.	N52364, N75135, N75421, W05142, W07655, AA029997, AA029107, AA463728
557441	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 420 of SEQ ID NO:38, b is an integer of 15 to 434, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:38, and where b is greater than or equal to a + 14.	
558091	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1064 of SEQ ID NO:39, b is an integer of 15 to 1078, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:39, and where b is greater than or equal to a + 14.	
558423	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1962 of SEQ ID NO:40, b is an integer of 15 to 1976, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:40, and where b is greater than or equal to a + 14.	T49968, R56305, H08010, H47549, N29144, N39902, N77470, N78717, AA182657, AA242919, AA252178
558465	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2296 of SEQ ID NO:41, b is an integer of 15 to 2310, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:41, and where b is greater than or equal to a + 14.	T85937, T96679, T96794, R13767, R14771, R38610, R42541, R42541, R60238, R60472, H14363, H14409, R94149, N30062, N30065, N40770, N92651, N92649, N99584, N99587, W37817
558493	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 392 of SEQ ID NO:42, b is an integer of 15 to 406, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:42, and where b is greater than or equal to a + 14.	
558778	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	

	sequence described by the general formula of a-b, where a is any integer between 1 to 613 of SEQ ID NO:43, b is an integer of 15 to 627, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:43, and where b is greater than or equal to a + 14.	
558818	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 731 of SEQ ID NO:44, b is an integer of 15 to 745, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:44, and where b is greater than or equal to a + 14.	
563182	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 453 of SEQ ID NO:45, b is an integer of 15 to 467, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:45, and where b is greater than or equal to a + 14.	
572571	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 708 of SEQ ID NO:46, b is an integer of 15 to 722, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:46, and where b is greater than or equal to a + 14.	R07415, R02207, H14209
575525	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 988 of SEQ ID NO:47, b is an integer of 15 to 1002, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:47, and where b is greater than or equal to a + 14.	R52330, H20661
580659	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2105 of SEQ ID NO:48, b is an integer of 15 to 2119, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:48, and where b is greater than or equal to a + 14.	
583650	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 480 of SEQ ID NO:49, b is an integer of 15 to 494, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:49, and where b is greater than or equal to a + 14.	
584698	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b.	

	where a is any integer between 1 to 1328 of SEQ ID NO:50, b is an integer of 15 to 1342, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:50, and where b is greater than or equal to a + 14.	
585791	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1513 of SEQ ID NO:51, b is an integer of 15 to 1527, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:51, and where b is greater than or equal to a + 14.	T48321, T67802, T67948, T67040, T67041, T83908, R09529, R09642, T83737, R16473, R16773, R25443, R26269, H05343, H26912, H28048, H39855, R86113, N33097, N44668, N79489, W16656, W60696, W60757, AA081126, AA081151, AA083763, AA132950, AA132862, AA149302, AA149416, AA191527, AA194936, AA195535, AA233905, AA234134
587229	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 616 of SEQ ID NO:52, b is an integer of 15 to 630, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:52, and where b is greater than or equal to a + 14.	
587246	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 561 of SEQ ID NO:53, b is an integer of 15 to 575, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:53, and where b is greater than or equal to a + 14.	
587486	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2920 of SEQ ID NO:54, b is an integer of 15 to 2934, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:54, and where b is greater than or equal to a + 14.	T71052, T71121, T72185, R21828, R21895, N51506, N53649, N66770, W72635, W77877, AA063260, AA083833, AA165549, AA165652, AA169616, AA256205, AA256348, AA464908
589218	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 561 of SEQ ID NO:55, b is an integer of 15 to 575, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:55, and where b is greater than or equal to a + 14.	R31110, N36905, N36910, N48189, W32216, AA069678, AA173954
592154	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1126 of SEQ ID NO:56, b is an integer of 15 to 1140, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:56, and where b is greater than or equal to a + 14.	R12094, T66653, T80236, R15999, R25029, R35910, AA194354
598664	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	W40222

	sequence described by the general formula of a-b, where a is any integer between 1 to 241 of SEQ ID NO:57, b is an integer of 15 to 255, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:57, and where b is greater than or equal to a + 14.	
598665	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1240 of SEQ ID NO:58, b is an integer of 15 to 1254, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:58, and where b is greater than or equal to a + 14.	W39277, W39349, W39357, W39764, W39767, W40288, W40538, W44820, W45264, W51936, W51937, W51918, W52848, W74327
604719	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1176 of SEQ ID NO:59, b is an integer of 15 to 1190, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:59, and where b is greater than or equal to a + 14.	T49228, T49490, T70505, T70428, T73981, T86568, T86746, T91867, R10309, R12088, T79988, T80222, T84402, T85263, T85576, T85577, R05432, R13226, R13278, R13833, R18842, R19462, R21598, R22718, R35298, H10723, H11136, H44767, R88961, R92868, R92897, R97874, H71254, H71922, H78937, H79825, H79920, H80125, H86893, H90187, N25116, N44644, N50007, N53591, N72554, W40421, W42525, W52370, AA021224, AA037505, AA053988
612689	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 566 of SEQ ID NO:60, b is an integer of 15 to 580, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:60, and where b is greater than or equal to a + 14.	H54589, AA227410
612980	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 439 of SEQ ID NO:61, b is an integer of 15 to 453, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:61, and where b is greater than or equal to a + 14.	
615134	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2579 of SEQ ID NO:62, b is an integer of 15 to 2593, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:62, and where b is greater than or equal to a + 14.	T54861, T55025, T92712, T92716, T92721, T92789, T92795, T92801, T92938, T93055, T93331, T94009, R15352, R25472, R26297, R33615, R33726, R53088, R62766, R62767, R71478, R71526, R78919, R79016, H06272, H06317, H24935, H24973, H28559, H28560, H42644, H38452, H38491, H47593, H47673, R87481, R88156, R89767, R89789, H51597, H57134, H57205, H62215, H62312, H97605, N24503, N27658, N35013, N43767, N92918, W15223, W39515, W72421, W76280, W86384,

		AA031688, AA031689, AA036840, AA045285, AA046566, AA099284, AA132058, AA132202, AA150688, AA150860, AA156675, AA159469, AA160880, AA165451, AA165638, AA173528, AA173712, AA458903, AA459097
616064	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1181 of SEQ ID NO:63, b is an integer of 15 to 1195, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:63, and where b is greater than or equal to a + 14.	
616096	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 378 of SEQ ID NO:64, b is an integer of 15 to 392, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:64, and where b is greater than or equal to a + 14.	
616926	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1276 of SEQ ID NO:65, b is an integer of 15 to 1290, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:65, and where b is greater than or equal to a + 14.	AA149936, AA150476, AA167701, AA167815, AA256842, AA256431, AA458750
634923	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 702 of SEQ ID NO:66, b is an integer of 15 to 716, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:66, and where b is greater than or equal to a + 14.	
646688	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1112 of SEQ ID NO:67, b is an integer of 15 to 1126, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:67, and where b is greater than or equal to a + 14.	
647531	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2125 of SEQ ID NO:68, b is an integer of 15 to 2139, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:68, and where b is greater than or equal to a + 14.	
647695	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	W52753, W60008, W60952, W73125

	sequence described by the general formula of a-b, where a is any integer between 1 to 1327 of SEQ ID NO:69, b is an integer of 15 to 1341, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:69, and where b is greater than or equal to a + 14.	
647699	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 721 of SEQ ID NO:70, b is an integer of 15 to 735, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:70, and where b is greater than or equal to a + 14.	
651706	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2016 of SEQ ID NO:71, b is an integer of 15 to 2030, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:71, and where b is greater than or equal to a + 14.	T71695, T71768, R08204, R08255, R31484, R31485, R50842, R52642, R53297, R60059, R60122, R60247, R60760, R62567, R62568, R70726, R71415, H38156, R83081, R94374, R94394, H53235, H60439, H60485, H63520, H63921, H64892, H65484, H71929, H77840, H77887, H78275, H79162, H80573, H94710, H95076, H95259, H95309, N46854, N47172, N49873, N55275, N64845, N68747, N74193, N74236, N91640, W01175, W01240, W57593, AA129298, AA129339, AA133183, AA133370
651726	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1861 of SEQ ID NO:72, b is an integer of 15 to 1875, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:72, and where b is greater than or equal to a + 14.	T90733, R10849, R10850, T82138, T83264, R87054, R91713, H71337, H71389, H72382, N55250, N74908, N76660, N76857, W20174, W23436, W35129, AA045320, AA045221
652160	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 846 of SEQ ID NO:73, b is an integer of 15 to 860, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:73, and where b is greater than or equal to a + 14.	
654015	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 506 of SEQ ID NO:74, b is an integer of 15 to 520, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:74, and where b is greater than or equal to a + 14.	
656339	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 849 of SEQ ID NO:75, b is an integer of 15 to 863, where both a and	H70078

	b correspond to the positions of nucleotide residues shown in SEQ ID NO:75, and where b is greater than or equal to a + 14.	
657190	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 677 of SEQ ID NO:76, b is an integer of 15 to 691, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:76, and where b is greater than or equal to a + 14.	
657859	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 311 of SEQ ID NO:77, b is an integer of 15 to 325, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:77, and where b is greater than or equal to a + 14.	
662143	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 807 of SEQ ID NO:78, b is an integer of 15 to 821, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:78, and where b is greater than or equal to a + 14.	R27497, R33219, R94577, N95517
662212	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 603 of SEQ ID NO:79, b is an integer of 15 to 617, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:79, and where b is greater than or equal to a + 14.	
662225	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1175 of SEQ ID NO:80, b is an integer of 15 to 1189, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:80, and where b is greater than or equal to a + 14.	R59488, H11016, N29502, AA025624
662496	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 452 of SEQ ID NO:81, b is an integer of 15 to 466, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:81, and where b is greater than or equal to a + 14.	
669529	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 346 of SEQ ID NO:82, b is an integer of 15 to 360, where both a and b correspond to the positions of nucleotide residues	

	shown in SEQ ID NO:82. and where b is greater than or equal to a + 14.	
670453	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2095 of SEQ ID NO:83. b is an integer of 15 to 2109, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:83. and where b is greater than or equal to a + 14.	T77608, R09248, R09364, R11470, R19371, R39244, H15039, H15949, H27001, H30603, H37983, R84579, R85044, R85045, R85469, H85744, H99185, N24468, N52798, N68992, N76620, W15294, W39329, W52841, W95437, W95781, AA057725, AA059439
675028	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1521 of SEQ ID NO:84. b is an integer of 15 to 1535, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:84. and where b is greater than or equal to a + 14.	T48289, T77554, R05507, R25405, R31496, R32660, R41978, R41978, R62600, R62648, R63390, R63445, R68659, R68711, R68771, R68865, H01655, H01656, H04239, R92875, R93091, H83742, H83886, H89969, N30705, N64395, N64408, N66492, N67310, N68265, N80959, N92190, W79008, W80400, N90831, AA075349, AA075461, AA224356
681325	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 417 of SEQ ID NO:85. b is an integer of 15 to 431, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:85. and where b is greater than or equal to a + 14.	
683103	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1128 of SEQ ID NO:86. b is an integer of 15 to 1142, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:86. and where b is greater than or equal to a + 14.	
684432	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1783 of SEQ ID NO:87. b is an integer of 15 to 1797, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:87. and where b is greater than or equal to a + 14.	R52639, R53294, R71671, R71703, H40352, H40408, R96789, R97034, R97271, R97719, H49468, H49467, H56659, H56739, H59341, H59998, H63308, H93861, H94642, H94643, N30295, N31741, N31742, N42019, N42450, N53570, N53844, N63677, N64865, N70725, N72529, N73341, N92110, N92116, N99031, W16862, W39154, W86457, N89634, AA005356, AA007379, AA235011, AA236270, AA253267
688018	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 367 of SEQ ID NO:88. b is an integer of 15 to 381, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:88. and where b is greater than or equal to a + 14.	T54297
688077	Preferably excluded from the present invention are	H00845, H01228, R95095, N76784.

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 524 of SEQ ID NO:89, b is an integer of 15 to 538, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.	N98607, W24232, W52082, W56721, W56767, W67714, W68173, W90739, W90774, AA033634, AA034341, AA062620, AA062994, AA258212
691522	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2107 of SEQ ID NO:90, b is an integer of 15 to 2121, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.	
693706	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2960 of SEQ ID NO:91, b is an integer of 15 to 2974, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:91, and where b is greater than or equal to a + 14.	T78218, T81634, R13915, R18080, H18055, H63131, H67579, AA035361, AA069801, AA069848, AA076182, AA079495, AA082095, AA102007, AA100775, AA143208, AA143346, AA146711, AA147300, AA180012, AA235098
694523	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 398 of SEQ ID NO:92, b is an integer of 15 to 412, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.	
697517	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1869 of SEQ ID NO:93, b is an integer of 15 to 1883, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:93, and where b is greater than or equal to a + 14.	T90609, AA053480, AA074689, AA102775, AA122090, AA182511, AA243116
699054	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2297 of SEQ ID NO:94, b is an integer of 15 to 2311, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:94, and where b is greater than or equal to a + 14.	
699464	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 500 of SEQ ID NO:95, b is an integer of 15 to 514, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:95, and where b is greater than or equal to a + 14.	T82960
703402	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	

	sequence described by the general formula of a-b, where a is any integer between 1 to 451 of SEQ ID NO:96, b is an integer of 15 to 465, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:96, and where b is greater than or equal to a + 14.	
703651	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1445 of SEQ ID NO:97, b is an integer of 15 to 1459, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:97, and where b is greater than or equal to a + 14.	
704905	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 865 of SEQ ID NO:98, b is an integer of 15 to 879, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:98, and where b is greater than or equal to a + 14.	
706907	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 234 of SEQ ID NO:99, b is an integer of 15 to 248, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:99, and where b is greater than or equal to a + 14.	
708515	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 466 of SEQ ID NO:100, b is an integer of 15 to 480, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:100, and where b is greater than or equal to a + 14.	R35145, H20357, H25361, H40070, N24435, N56688, W92201, AA164775
710572	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 439 of SEQ ID NO:101, b is an integer of 15 to 453, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:101, and where b is greater than or equal to a + 14.	AA188988, AA188989
710618	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 889 of SEQ ID NO:102, b is an integer of 15 to 903, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:102, and where b is greater than or equal to a + 14.	T92687, N50744
711810	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b.	

	where a is any integer between 1 to 1774 of SEQ ID NO:103, b is an integer of 15 to 1788, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:103, and where b is greater than or equal to a + 14.	
714933	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3305 of SEQ ID NO:104, b is an integer of 15 to 3319, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:104, and where b is greater than or equal to a + 14.	T65559, T65626, R10350, R13281, R13569, R14670, R15257, R34544, R36053, R39872, R40726, R49062, R49135, R53355, R53957, R49062, R49135, R40726, R78042, H05306, H05356, H07035, H10902, H14308, H24047, H24154, R89696, R93433, R98651, R98650, H50887, H53389, H91935, H91944, H99472, N25040, N26192, N28285, N48283, N49011, N62360, N68609, N71824, N79127, W72510, W76067, W94862, W94822, W96008, W96040, AA025005, AA036767, AA044132, AA044098, AA047829, AA047855, AA054452, AA054567, AA057171, AA085624, AA088811, AA130768, AA130944, AA132373, AA132618, AA150892, AA151019, AA157288, AA157368, AA157369, AA159896, AA160826, AA180535, AA187424, AA187614
716331	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1972 of SEQ ID NO:105, b is an integer of 15 to 1986, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:105, and where b is greater than or equal to a + 14.	
717686	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 577 of SEQ ID NO:106, b is an integer of 15 to 591, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:106, and where b is greater than or equal to a + 14.	
718187	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 139 of SEQ ID NO:107, b is an integer of 15 to 153, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:107, and where b is greater than or equal to a + 14.	
719934	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1522 of SEQ ID NO:108, b is an integer of 15 to 1536, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:108, and where b is	

	greater than or equal to $a + 14$.	
722980	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 498 of SEQ ID NO:109, b is an integer of 15 to 512, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:109, and where b is greater than or equal to $a + 14$.	
723596	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1441 of SEQ ID NO:110, b is an integer of 15 to 1455, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:110, and where b is greater than or equal to $a + 14$.	W90706, W95592, AA047652, AA250970, AA250874, AA251071, AA251074, AA251073
724352	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 661 of SEQ ID NO:111, b is an integer of 15 to 675, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:111, and where b is greater than or equal to $a + 14$.	
724450	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 534 of SEQ ID NO:112, b is an integer of 15 to 548, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:112, and where b is greater than or equal to $a + 14$.	
724855	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 462 of SEQ ID NO:113, b is an integer of 15 to 476, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:113, and where b is greater than or equal to $a + 14$.	T77137, T88762, T99291, R07006, AA004532
724904	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1002 of SEQ ID NO:114, b is an integer of 15 to 1016, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:114, and where b is greater than or equal to $a + 14$.	
725642	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 480 of SEQ ID NO:115, b is an integer of 15 to 494, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:115, and where b is greater than or equal to $a + 14$.	

726192	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3222 of SEQ ID NO:116, b is an integer of 15 to 3236, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:116, and where b is greater than or equal to a + 14.	T65882, T66040, T77662, R53239, R59914, R59915, R62156, R62264, R63487, H04945, H04951, H13535, H13536, H16274, N25318, N25787, N31430, N32153, N36498, N49086, N49333, N50212, N66885, N78949, AA115267, AA115291, AA150461, AA164418, AA195130, AA195277, AA234969, AA236191, AA251324, AA251530, AA251517, AA258562, AA258724
726964	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 897 of SEQ ID NO:117, b is an integer of 15 to 911, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:117, and where b is greater than or equal to a + 14.	
730930	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1963 of SEQ ID NO:118, b is an integer of 15 to 1977, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:118, and where b is greater than or equal to a + 14.	
731314	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 790 of SEQ ID NO:119, b is an integer of 15 to 804, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:119, and where b is greater than or equal to a + 14.	R32598, R36499
732386	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 723 of SEQ ID NO:120, b is an integer of 15 to 737, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:120, and where b is greater than or equal to a + 14.	AA417877, AA424537, AA424604
732909	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1238 of SEQ ID NO:121, b is an integer of 15 to 1252, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:121, and where b is greater than or equal to a + 14.	
733088	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1834 of SEQ ID NO:122, b is an integer of 15 to 1848, where both a and b correspond to the positions of nucleotide	

	residues shown in SEQ ID NO:122, and where b is greater than or equal to $a + 14$.	
733351	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 449 of SEQ ID NO:123, b is an integer of 15 to 463, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:123, and where b is greater than or equal to $a + 14$.	
733693	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 336 of SEQ ID NO:124, b is an integer of 15 to 350, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:124, and where b is greater than or equal to $a + 14$.	
734760	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1570 of SEQ ID NO:125, b is an integer of 15 to 1584, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:125, and where b is greater than or equal to $a + 14$.	T78350, T79874, R13714, H83297, H86534, N20546, N93623, N93932, W23965, AA016035, AA016080, AA017047, AA021630, AA046286, AA063218, AA076542, AA158847, AA159397, AA160406, AA213767, AA255605, AA422075, AA421997, AA424997
735711	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1290 of SEQ ID NO:126, b is an integer of 15 to 1304, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:126, and where b is greater than or equal to $a + 14$.	
742413	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 887 of SEQ ID NO:127, b is an integer of 15 to 901, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:127, and where b is greater than or equal to $a + 14$.	R99084, R99627
742676	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3273 of SEQ ID NO:128, b is an integer of 15 to 3287, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:128, and where b is greater than or equal to $a + 14$.	T40095, T40106, T40156, T41006, T46845, T46862, T46892, T51126, T51142, T51176, T51197, T53736, T53747, T53827, T53835, T53850, T53939, T53959, T55991, T56035, T56068, T56236, T56378, T57000, T57001, T58101, T58719, T58786, T58850, T58866, T58898, T58906, T58910, T58925, T58961, T60324, T60332, T60352, T60362, T60377, T60385, T60424, T60444, T60476, T60477, T60507, T60570, T60599, T60631, T61109, T61277, T61376, T61409, T61618, T61702, T61743, T61865, T61875, T62046, T62079.

	T62110. T62136. T39959. T47778. T47810. T53910. T61195. T61199. T61883. T62738. T62764. T62888. T62914. T64121. T64186. T64232. T64242. T64305. T64309. T64585. T64595. T64652. T64692. T64696. T64738. T64751. T67432. T67593. T67633. T67703. T67725. T67736. T67739. T67753. T67755. T67820. T67837. T67845. T67848. T67862. T67864. T67886. T67895. T67907. T67922. T67929. T67971. T68044. T68055. T68070. T68106. T68107. T68170. T68176. T68201. T68220. T68245. T68267. T68291. T68301. T68329. T68355. T68367. T68401. T68516. T68607. T68688. T68716. T68772. T68781. T68842. T68914. T69001. T69031. T69081. T69122. T69139. T69145. T69180. T69197. T69206. T69230. T69243. T69283. T69293. T69317. T69358. T69368. T69400. T69420. T69445. T70452. T70475. T70494. T70495. T70498. T70975. T71039. T71105. T71313. T71351. T71356. T71429. T71457. T71518. T71692. T71698. T71712. T71715. T71781. T71784. T71800. T71851. T71857. T71870. T71875. T71895. T71908. T71914. T71916. T71959. T72031. T72037. T72042. T72063. T72065. T72079. T72098. T72099. T72152. T72177. T72178. T72199. T72223. T72300. T72304. T72360. T72394. T72407. T72418. T72451. T72456. T72464. T72510. T72517. T72525. T72793. T72803. T72821. T72826. T72827. T72956. T72957. T72978. T73010. T73052. T73096. T73203. T73225. T73250. T73258. T73265. T73317. T73333. T73382. T73400. T73410. T73425. T73427. T73445. T73493. T73495. T73512. T73566. T73666. T73729. T73768. T73787. T73819. T73868. T73873. T73920. T73931. T73952. T73962. T74033. T74101. T74111. T74269. T74273. T74372. T74380. T74407. T74474. T74485. T74541. T74598. T74615. T74645. T74658. T74673. T74677. T74756. T74765. T74843. T74854. T74860. T74863. T74914. T71341. T71501. T77799. T90078. T82897. T95610. T95711. R02292. R02293. R06796. R95746. R98475. H48262. H48353. H58120. H58121. H61463. H67459. H70620.
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		H90426, H90482, H94389, N33594, N49440, N75535, W05328, W19064, W86031, AA011414, AA026625, AA026737, AA235252
742781	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1668 of SEQ ID NO:129, b is an integer of 15 to 1682, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:129, and where b is greater than or equal to a + 14.	R00982, R00983, R20611, R21647, R46119, R46119, H29203, H29204, N47470, N47471, N64818, N75670, N79512, N92805, W16709, AA023019, AA022493, AA143187, AA171546, AA233410, AA460731
743356	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 286 of SEQ ID NO:130, b is an integer of 15 to 300, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:130, and where b is greater than or equal to a + 14.	
745694	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 91 of SEQ ID NO:131, b is an integer of 15 to 105, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:131, and where b is greater than or equal to a + 14.	
747235	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 897 of SEQ ID NO:132, b is an integer of 15 to 911, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:132, and where b is greater than or equal to a + 14.	
750986	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3562 of SEQ ID NO:133, b is an integer of 15 to 3576, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:133, and where b is greater than or equal to a + 14.	
751068	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1179 of SEQ ID NO:134, b is an integer of 15 to 1193, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:134, and where b is greater than or equal to a + 14.	W23633, W35271, W86390, W86391
751164	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1931 of SEQ ID NO:135, b is an integer of 15 to 1945, where both a	

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:135, and where b is greater than or equal to $a + 14$.	
751890	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1132 of SEQ ID NO:136, b is an integer of 15 to 1146, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:136, and where b is greater than or equal to $a + 14$.	R12199, AA056402
751991	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2331 of SEQ ID NO:137, b is an integer of 15 to 2345, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:137, and where b is greater than or equal to $a + 14$.	
752449	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 717 of SEQ ID NO:138, b is an integer of 15 to 731, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:138, and where b is greater than or equal to $a + 14$.	H49093, H63940, H68327, H72930, H80397, N59075, N59482
752504	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 743 of SEQ ID NO:139, b is an integer of 15 to 757, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:139, and where b is greater than or equal to $a + 14$.	
752688	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 649 of SEQ ID NO:140, b is an integer of 15 to 663, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:140, and where b is greater than or equal to $a + 14$.	T83204, W07391
752889	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3921 of SEQ ID NO:141, b is an integer of 15 to 3935, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:141, and where b is greater than or equal to $a + 14$.	
753150	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2198 of SEQ ID NO:142, b is an integer of 15 to 2212, where both a and b correspond to the positions of nucleotide	

	residues shown in SEQ ID NO:142, and where b is greater than or equal to a + 14.	
753690	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 729 of SEQ ID NO:143, b is an integer of 15 to 743, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:143, and where b is greater than or equal to a + 14.	AA262521
754479	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 825 of SEQ ID NO:144, b is an integer of 15 to 839, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:144, and where b is greater than or equal to a + 14.	
754692	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2893 of SEQ ID NO:145, b is an integer of 15 to 2907, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:145, and where b is greater than or equal to a + 14.	
756814	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1823 of SEQ ID NO:146, b is an integer of 15 to 1837, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:146, and where b is greater than or equal to a + 14.	T51378, T54439, T54440, T54492, T39385, T89470, T89560, R05534, R05644, R17667, R25313, R32922, R33132, R33284, R35666, R35777, R38043, R38132, R38752, R43414, R54027, R54028, R43414, R63780, R64328, R64614, R64615, R74563, R82622, H01362, H01835, H02683, H02973, H04269, H09641, H09675, H10002, H13064, H13271, H13720, H13933, H13934, H15328, H15712, H15993, R83464, R83844, R83845, R89553, R95676, R97388, R98691, R98917, H48613, H48805, H51096, H51682, H58872, H58873, H67326, H68534, H70197, H78192, H78193, H79697, H79698, H83266, H83267, H90205, H90308, H90862, H90962, H94344, H95788, H96137, H97956, H99868, N28553, N68855, N94629, W31434, W31994, W46421, W52814, W56529, W56780, W58375, W58549, W58662, W68203, W68204, W69142, W69248, W81130, W81131, W81700, W81701, AA043367, AA043368, AA044067, AA044159, AA122334, AA464398, AA419080, AA423821, AA428882, AA428973, AA429196
757127	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	

	where a is any integer between 1 to 1357 of SEQ ID NO:147, b is an integer of 15 to 1371, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:147, and where b is greater than or equal to $a + 14$.	
757347	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1743 of SEQ ID NO:148, b is an integer of 15 to 1757, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:148, and where b is greater than or equal to $a + 14$.	
757495	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3518 of SEQ ID NO:149, b is an integer of 15 to 3532, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:149, and where b is greater than or equal to $a + 14$.	R24543, R24651, R25091, R36580, R45429, R51961, R53628, R45429, R64120, R64218, R67926, R69338, R69339, R74200, R74291, R80166, H00661, H00753, H02579, H02665, H64801, H64802, H64802, N63215, N75662, W46814, W46864, W70290, W72831, W72832, W75986, W90099, W90197, AA025841, AA025842, AA039870, AA040233, AA043893, AA042891, AA043018, AA062769, AA074082, AA075813, AA082428, AA196448, AA196691
757715	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1917 of SEQ ID NO:150, b is an integer of 15 to 1931, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:150, and where b is greater than or equal to $a + 14$.	R10018, T80752, T81225, R13945, H14918, H45144, N78192, W01185, W52734, W73106, W79308, AA043840, AA044358, AA064738, AA160313, AA196613, AA226860, AA232389
760388	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1617 of SEQ ID NO:151, b is an integer of 15 to 1631, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:151, and where b is greater than or equal to $a + 14$.	T71835, T94624, T82230, T96710, R23486, R23859, R26080, R36711, R37553, R38131, H87609, N26790, N41457, W24534, W31754, W31873, W32038, W32317, W32647, W38857, W39517, W39338, W56012, W56108, W56683, W57744, W72389, W76407, W93884, W93885, AA010989, AA160043, AA169520
760433	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 718 of SEQ ID NO:152, b is an integer of 15 to 732, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:152, and where b is greater than or equal to $a + 14$.	
760545	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 480 of SEQ ID NO:153, b is an integer of 15 to 494, where both a and b correspond to the positions of nucleotide	

	residues shown in SEQ ID NO:153, and where b is greater than or equal to a + 14.	
761566	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2427 of SEQ ID NO:154, b is an integer of 15 to 2441, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:154, and where b is greater than or equal to a + 14.	T69288, T69363, T94926, R12359, R26909, R27151, R37284, R61007, R61674, R68776, R68872, R70952, R71004, H92792, H92913, N25506, N32325, N57420, N68341, N94012, AA011440, AA076005, AA076006, AA129646, AA129781, AA187676
761740	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2933 of SEQ ID NO:155, b is an integer of 15 to 2947, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:155, and where b is greater than or equal to a + 14.	R13217, R30963, R31018, R40301, R51543, R51544, R40301, R63409, H29530, H83725, H98067, N20307, N27578, N28375, N46832, N62348, N62593, N78359, N79110, AA041460, AA041513, AA046252, AA046371, AA125849, AA125850, AA252450, AA461403
765215	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 652 of SEQ ID NO:156, b is an integer of 15 to 666, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:156, and where b is greater than or equal to a + 14.	T54662, T54749
765428	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 613 of SEQ ID NO:157, b is an integer of 15 to 627, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14.	
766686	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 888 of SEQ ID NO:158, b is an integer of 15 to 902, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14.	
767396	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 579 of SEQ ID NO:159, b is an integer of 15 to 593, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14.	AA172282, AA220915
767501	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1833 of SEQ ID NO:160, b is an integer of 15 to 1847, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:160, and where b is	T48254, T48253, T61610, T61695, T70390, T70397, T86348, R11405, R05486, R05593, R19155, R61228, R61229, R70142, R70143, R78897, R78993, R94037, N81160, W90480, W90479, W95079, AA192429

	greater than or equal to $a + 14$.	
767945	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 356 of SEQ ID NO:161, b is an integer of 15 to 370, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:161, and where b is greater than or equal to $a + 14$.	
768996	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 440 of SEQ ID NO:162, b is an integer of 15 to 454, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:162, and where b is greater than or equal to $a + 14$.	
771415	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1082 of SEQ ID NO:163, b is an integer of 15 to 1096, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:163, and where b is greater than or equal to $a + 14$.	
772657	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2009 of SEQ ID NO:164, b is an integer of 15 to 2023, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:164, and where b is greater than or equal to $a + 14$.	T39789, R21583, R23570, R63603, R63604, R80168, R80167, H02287, H02391, N25705, N26310, N26346, N34095, N39754, N51681, N91936, W24114, AA035390, AA035389, AA043307, AA043308, AA043279, AA043280, AA053303, AA058551, AA082488, AA122113, AA142961, AA149350, AA149351, AA150613, AA150739, AA150847, AA179036, AA251541, AA251499
773123	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1306 of SEQ ID NO:165, b is an integer of 15 to 1320, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:165, and where b is greater than or equal to $a + 14$.	
773193	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1191 of SEQ ID NO:166, b is an integer of 15 to 1205, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:166, and where b is greater than or equal to $a + 14$.	
773710	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1399 of SEQ ID NO:167, b is an integer of 15 to 1413, where both a	T91089, T84760, R18409, R42472, R44656, R42472, R44656, R70650, H94730, H94759, N30658, N66021, N66027, N66688, N95136, N98956, AA131377, AA131494, AA131593,

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:167, and where b is greater than or equal to a + 14.	AA131658, AA227712, AA227958, AA424025
774283	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1214 of SEQ ID NO:168, b is an integer of 15 to 1228, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:168, and where b is greater than or equal to a + 14.	R81621, H75455, H75454, AA165108, AA164711, AA461410, AA461095
774369	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1911 of SEQ ID NO:169, b is an integer of 15 to 1925, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:169, and where b is greater than or equal to a + 14.	R26376, R66765, H86185, AA016184, AA021102, AA028914, AA133277, AA133354
774754	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1544 of SEQ ID NO:170, b is an integer of 15 to 1558, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:170, and where b is greater than or equal to a + 14.	W38589, W74674, W74780, N90213, AA043957, AA043823, AA157016
774823	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1388 of SEQ ID NO:171, b is an integer of 15 to 1402, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:171, and where b is greater than or equal to a + 14.	
775510	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 476 of SEQ ID NO:172, b is an integer of 15 to 490, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:172, and where b is greater than or equal to a + 14.	
775634	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1423 of SEQ ID NO:173, b is an integer of 15 to 1437, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:173, and where b is greater than or equal to a + 14.	
775640	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1801 of SEQ ID NO:174, b is an integer of 15 to 1815, where both a and b correspond to the positions of nucleotide	

	residues shown in SEQ ID NO:174, and where b is greater than or equal to $a + 14$.	
775802	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 957 of SEQ ID NO:175, b is an integer of 15 to 971, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:175, and where b is greater than or equal to $a + 14$.	
777470	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1608 of SEQ ID NO:176, b is an integer of 15 to 1622, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:176, and where b is greater than or equal to $a + 14$.	R72009, R81577, H26684, H45155, R87903, R87922, W46492, W51858
777652	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 326 of SEQ ID NO:177, b is an integer of 15 to 340, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:177, and where b is greater than or equal to $a + 14$.	
778998	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 602 of SEQ ID NO:178, b is an integer of 15 to 616, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:178, and where b is greater than or equal to $a + 14$.	
779273	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2053 of SEQ ID NO:179, b is an integer of 15 to 2067, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:179, and where b is greater than or equal to $a + 14$.	
779297	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1813 of SEQ ID NO:180, b is an integer of 15 to 1827, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:180, and where b is greater than or equal to $a + 14$.	T58639, T58688, T65114, T65181, T79935, R37097, H01720, H93130, N49316, N49558, W32803, W95634, AA025739, AA426310, AA428778
779664	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1012 of SEQ ID NO:181, b is an integer of 15 to 2026, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:181, and where b is	T91627, R18325, R37374, R59694, R60216, R60450, H28798, H28818, N30799, N39412, W74507, W79219, AA083583, AA135148, AA164254, AA164365, AA172128

	greater than or equal to $a + 14$.	
780565	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 442 of SEQ ID NO:182, b is an integer of 15 to 456, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:182, and where b is greater than or equal to $a + 14$.	
780665	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 467 of SEQ ID NO:183, b is an integer of 15 to 481, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:183, and where b is greater than or equal to $a + 14$.	W60277
780666	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 482 of SEQ ID NO:184, b is an integer of 15 to 496, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:184, and where b is greater than or equal to $a + 14$.	
781579	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1293 of SEQ ID NO:185, b is an integer of 15 to 1307, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:185, and where b is greater than or equal to $a + 14$.	T57785, T82345, W86564, AA078858, AA155901, AA161451, AA178927, AA194606
782052	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 435 of SEQ ID NO:186, b is an integer of 15 to 449, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:186, and where b is greater than or equal to $a + 14$.	
782393	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 937 of SEQ ID NO:187, b is an integer of 15 to 951, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:187, and where b is greater than or equal to $a + 14$.	N25688, N30017, N34076, N36364, N46861, N47181, N62606, N92811, W24930, W25337, W47158, W47279, W49821, AA234682, AA234755, AA252206
782907	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 367 of SEQ ID NO:188, b is an integer of 15 to 381, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:188, and where b is greater than or equal to $a + 14$.	

783220	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1295 of SEQ ID NO:189, b is an integer of 15 to 1309, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:189, and where b is greater than or equal to a + 14.	
783300	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1885 of SEQ ID NO:190, b is an integer of 15 to 1899, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:190, and where b is greater than or equal to a + 14.	
783938	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2476 of SEQ ID NO:191, b is an integer of 15 to 2490, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:191, and where b is greater than or equal to a + 14.	
784024	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1794 of SEQ ID NO:192, b is an integer of 15 to 1808, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:192, and where b is greater than or equal to a + 14.	H89685, N20336, N27611, N31596, N42655, N51849, N51859, N62943, AA236316, AA253217
784575	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1059 of SEQ ID NO:193, b is an integer of 15 to 1073, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:193, and where b is greater than or equal to a + 14.	
785006	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 373 of SEQ ID NO:194, b is an integer of 15 to 387, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:194, and where b is greater than or equal to a + 14.	
785069	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 959 of SEQ ID NO:195, b is an integer of 15 to 973, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:195, and where b is greater than or equal to a + 14.	
785237	Preferably excluded from the present invention are	

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 629 of SEQ ID NO:196, b is an integer of 15 to 643, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:196, and where b is greater than or equal to a + 14.	
786111	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 438 of SEQ ID NO:197, b is an integer of 15 to 452, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:197, and where b is greater than or equal to a + 14.	
787036	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1018 of SEQ ID NO:198, b is an integer of 15 to 1032, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:198, and where b is greater than or equal to a + 14.	R11814, H14163, N42713, W69844, AA076578
788991	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2718 of SEQ ID NO:199, b is an integer of 15 to 2732, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:199, and where b is greater than or equal to a + 14.	T94446, T94533, R12065, R13249, R13635, R38488, R40329, R43592, R46434, R43592, R40329, H16332, H20990, H28489, H29906, H39987, R83899, R85669, R85905, H57115, H89691, W01303, W03530, W44921, W52157, AA001492, AA001493, AA054074, AA054263, AA059205, AA059263, AA461201, AA461378, AA417279, AA417269, AA429343
789125	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2301 of SEQ ID NO:200, b is an integer of 15 to 2315, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:200, and where b is greater than or equal to a + 14.	
789626	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 876 of SEQ ID NO:201, b is an integer of 15 to 890, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:201, and where b is greater than or equal to a + 14.	
789703	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1519 of SEQ ID NO:202, b is an integer of 15 to 1533, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:202, and where b is greater than or equal to a + 14.	

789858	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2812 of SEQ ID NO:203, b is an integer of 15 to 2826, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:203, and where b is greater than or equal to a + 14.	
790848	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1524 of SEQ ID NO:204, b is an integer of 15 to 1538, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:204, and where b is greater than or equal to a + 14.	R62582, R62583, N45584, N48793, N49502.
790893	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2328 of SEQ ID NO:205, b is an integer of 15 to 2342, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:205, and where b is greater than or equal to a + 14.	
790912	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 813 of SEQ ID NO:206, b is an integer of 15 to 827, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:206, and where b is greater than or equal to a + 14.	T79209, R46211, H05016, H25436, AA236254, AA236301
791386	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2312 of SEQ ID NO:207, b is an integer of 15 to 2326, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:207, and where b is greater than or equal to a + 14.	
791598	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1448 of SEQ ID NO:208, b is an integer of 15 to 1462, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:208, and where b is greater than or equal to a + 14.	
791619	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2567 of SEQ ID NO:209, b is an integer of 15 to 2581, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:209, and where b is greater than or equal to a + 14.	R14767, R25924, R42537, R42537, R61122, R61844, H60027, H67016, W58641, W58640
791628	Preferably excluded from the present invention are	

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1980 of SEQ ID NO:210, b is an integer of 15 to 1994, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:210, and where b is greater than or equal to a + 14.	
791751	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1500 of SEQ ID NO:211, b is an integer of 15 to 1514, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:211, and where b is greater than or equal to a + 14.	R09808, R68694, N32219, W63661, AA040449, AA234814, AA235276
792557	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 469 of SEQ ID NO:212, b is an integer of 15 to 483, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:212, and where b is greater than or equal to a + 14.	AA056147
792568	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 869 of SEQ ID NO:213, b is an integer of 15 to 883, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:213, and where b is greater than or equal to a + 14.	
792590	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4785 of SEQ ID NO:214, b is an integer of 15 to 4799, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:214, and where b is greater than or equal to a + 14.	T64783, T72536, T80095, R13317, R18856, R24593, R40794, R44398, R44398, R40794, R75943, R76782, H84406, H84405, N26104, N26704, N34584, N36742, N36957, N46274, N48855, N53045, N67252, N73229, N75830, W07313, W38467, N90066, AA057494, AA187860, AA187859, AA253007, AA253130, AA258718, AA425229, AA425655
793323	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1031 of SEQ ID NO:215, b is an integer of 15 to 1045, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:215, and where b is greater than or equal to a + 14.	T55304, T58854, T61562, T90445, R07868, R07924, T66596, T78891, T82882, R15970, R32044, R32101, R56409, R64171, R64286, R71032, R71031, R77398, R77397, R79661, R79851, H26905, H47068, H47147, H47364, H48041, R92212, R92317, R95919, H50513, H51351, H52213, H52215, H57893, H57894, H61850, H79743, H79744, H82302, H85765, H94322, H94414, N20359, N25613, N26068, N34211, N35221, N40430, N54905, N62582, N69480, N70945, N74352, N74406, N75952, N76289, N80355, W02619, W04976, N90972, AA127903, AA459690, AA459811

793466	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1150 of SEQ ID NO:216, b is an integer of 15 to 1164, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:216, and where b is greater than or equal to a + 14.	
793507	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1580 of SEQ ID NO:217, b is an integer of 15 to 1594, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:217, and where b is greater than or equal to a + 14.	T68445, T68510, H11722, N54260, N64522, N80313, W74096, W79387, AA147027, AA426623, AA424798
793546	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1531 of SEQ ID NO:218, b is an integer of 15 to 1545, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:218, and where b is greater than or equal to a + 14.	
793559	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 448 of SEQ ID NO:219, b is an integer of 15 to 462, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:219, and where b is greater than or equal to a + 14.	
793604	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3080 of SEQ ID NO:220, b is an integer of 15 to 3094, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:220, and where b is greater than or equal to a + 14.	T64153, T64282, T94117, T94206, T87138, T81405, T81406, T85085, T86057, T97192, R01163, R06234, R14694, R14930, R32761, R32762, R41244, R42415, R52098, R52193, R41244, R42415, H10037, H10091, H11045, H11133, H24727, H24726, H24776, H24823, H26838, H44556, H44557, H61794, H61795, H83904, N28677, N32272, N37013, N40509, N46458, N57996, W51862, W73372, W73433, AA024892, AA024891, AA029877, AA029113, AA031341, AA036870, AA044325, AA044578, AA054735, AA054742, AA069699, AA084245, AA084244, AA120803, AA120804, AA227168, AA235731, AA459397, AA459622, AA464006, AA464713, AA425178, AA429092
794121	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1742 of SEQ ID NO:221, b is an integer of 15 to 1756, where both a and b correspond to the positions of nucleotide	

	residues shown in SEQ ID NO:221, and where b is greater than or equal to a + 14.	
794295	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 557 of SEQ ID NO:222, b is an integer of 15 to 571, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:222, and where b is greater than or equal to a + 14.	H62096, AA021403, AA224005
795241	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1683 of SEQ ID NO:223, b is an integer of 15 to 1697, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:223, and where b is greater than or equal to a + 14.	
795286	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2142 of SEQ ID NO:224, b is an integer of 15 to 2156, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:224, and where b is greater than or equal to a + 14.	T80215, T80216, R13602, R17713, R38783, R38784, R39897, R41783, R41783, R61528, R61584, H13658, H13659, H14690, H20561, H20654, H20770, H22585, R87081, R88769, R91028, R94865, R94866, N31866, N33177, N34225, N44964, N45304, N51118, N54239, N70835, W01441, W74260, W79873, W86917, W86947, W92091, AA010531, AA010532, AA011408, AA011464, AA130389, AA215587
795637	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1777 of SEQ ID NO:225, b is an integer of 15 to 1791, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:225, and where b is greater than or equal to a + 14.	
796301	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1511 of SEQ ID NO:226, b is an integer of 15 to 1525, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:226, and where b is greater than or equal to a + 14.	R05274, R86959, N55553, N76938, AA039578, AA042797, AA044610, AA243346, AA243547, AA262732, AA262814
796347	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1597 of SEQ ID NO:227, b is an integer of 15 to 1611, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:227, and where b is greater than or equal to a + 14.	
796579	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	T39155, T40439, T65119, T65188, R61110, R61832, H00285, H00286, H08348, H08349, N24725, N36706.

	where a is any integer between 1 to 1625 of SEQ ID NO:228, b is an integer of 15 to 1639, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:228, and where b is greater than or equal to a + 14.	N44806, N52179, N59471, N63112, N66486, N72051, W68534, W68821, W95493, W95530, AA055460, AA165066, AA164670, AA172036, AA172288, AA224152, AA256292, AA256434
796590	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1069 of SEQ ID NO:229, b is an integer of 15 to 1083, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:229, and where b is greater than or equal to a + 14.	
799783	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 345 of SEQ ID NO:230, b is an integer of 15 to 359, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:230, and where b is greater than or equal to a + 14.	
799784	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 341 of SEQ ID NO:231, b is an integer of 15 to 355, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:231, and where b is greater than or equal to a + 14.	
799785	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 360 of SEQ ID NO:232, b is an integer of 15 to 374, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:232, and where b is greater than or equal to a + 14.	
799786	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 418 of SEQ ID NO:233, b is an integer of 15 to 432, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:233, and where b is greater than or equal to a + 14.	
799787	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 352 of SEQ ID NO:234, b is an integer of 15 to 366, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:234, and where b is greater than or equal to a + 14.	
799800	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b.	

	where a is any integer between 1 to 414 of SEQ ID NO:235, b is an integer of 15 to 428, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:235, and where b is greater than or equal to a + 14.	
799808	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 952 of SEQ ID NO:236, b is an integer of 15 to 966, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:236, and where b is greater than or equal to a + 14.	W38424, W38440, W39289, W40123, W40239, W40423, W40223, W44752, W44840, W45263, W45310, W45466, W45478, W45484, W52088, W52399, W52587, W52966, W56192, W59966, W60273, W60443, W60621, W74243
799977	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 683 of SEQ ID NO:237, b is an integer of 15 to 697, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:237, and where b is greater than or equal to a + 14.	
800149	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2253 of SEQ ID NO:238, b is an integer of 15 to 2267, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:238, and where b is greater than or equal to a + 14.	
800189	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 753 of SEQ ID NO:239, b is an integer of 15 to 767, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:239, and where b is greater than or equal to a + 14.	
800589	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1704 of SEQ ID NO:240, b is an integer of 15 to 1718, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:240, and where b is greater than or equal to a + 14.	
800811	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3585 of SEQ ID NO:241, b is an integer of 15 to 3599, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:241, and where b is greater than or equal to a + 14.	
800857	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2873 of SEQ ID	

	NO:242. b is an integer of 15 to 2887. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:242. and where b is greater than or equal to a + 14.	
805721	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1239 of SEQ ID NO:243. b is an integer of 15 to 1253. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:243. and where b is greater than or equal to a + 14.	
805818	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1588 of SEQ ID NO:244. b is an integer of 15 to 1602. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:244. and where b is greater than or equal to a + 14.	R37467, R43162, R49031, R43162, H90387, AA161488
806267	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1270 of SEQ ID NO:245. b is an integer of 15 to 1284. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:245. and where b is greater than or equal to a + 14.	
806579	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2080 of SEQ ID NO:246. b is an integer of 15 to 2094. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:246. and where b is greater than or equal to a + 14.	
810625	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1005 of SEQ ID NO:247. b is an integer of 15 to 1019. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:247. and where b is greater than or equal to a + 14.	
811153	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1486 of SEQ ID NO:248. b is an integer of 15 to 1500. where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:248. and where b is greater than or equal to a + 14.	
811787	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2287 of SEQ ID NO:249. b is an integer of 15 to 2301. where both a	

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:249, and where b is greater than or equal to $a + 14$.	
812314	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2103 of SEQ ID NO:250, b is an integer of 15 to 2117, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:250, and where b is greater than or equal to $a + 14$.	
812443	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1432 of SEQ ID NO:251, b is an integer of 15 to 1446, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:251, and where b is greater than or equal to $a + 14$.	
812498	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2036 of SEQ ID NO:252, b is an integer of 15 to 2050, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:252, and where b is greater than or equal to $a + 14$.	
812504	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2515 of SEQ ID NO:253, b is an integer of 15 to 2529, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:253, and where b is greater than or equal to $a + 14$.	
813079	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1664 of SEQ ID NO:254, b is an integer of 15 to 1678, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:254, and where b is greater than or equal to $a + 14$.	
815889	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 952 of SEQ ID NO:255, b is an integer of 15 to 966, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:255, and where b is greater than or equal to $a + 14$.	R75777, R81161, H89597, N66387, AA031510, AA031511, AA046590, AA046523, AA114840, AA114841, AA262053, AA459986, AA460079
824358	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3077 of SEQ ID NO:256, b is an integer of 15 to 3091, where both a and b correspond to the positions of nucleotide	

	residues shown in SEQ ID NO:256. and where b is greater than or equal to a + 14.	
826144	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2938 of SEQ ID NO:257, b is an integer of 15 to 2952, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:257, and where b is greater than or equal to a + 14.	T49872, R13469, R14630, R37379, R53048, R53135, R66676, R67394, R68165, R73097, R73098, H05459, H07010, H10504, H14581, H14671, H54297, H54374, H60845, H60931, H67688, H68011, N20226, N21171, N26851, N29134, N29294, N29562, N42173, AA026121, AA026205, AA136924, AA137020, AA460265, AA463830
826558	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2203 of SEQ ID NO:258, b is an integer of 15 to 2217, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:258, and where b is greater than or equal to a + 14.	T93500, R30805, R34197, R66925, R66924, H00931, H01734, H02282, H02385, W52225, AA040653, AA045530, AA058953, AA059458, AA127997, AA128093
827471	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1226 of SEQ ID NO:259, b is an integer of 15 to 1240, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:259, and where b is greater than or equal to a + 14.	
827716	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 596 of SEQ ID NO:260, b is an integer of 15 to 610, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:260, and where b is greater than or equal to a + 14.	
827722	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2102 of SEQ ID NO:261, b is an integer of 15 to 2116, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:261, and where b is greater than or equal to a + 14.	
827727	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1543 of SEQ ID NO:262, b is an integer of 15 to 1557, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:262, and where b is greater than or equal to a + 14.	
828238	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1640 of SEQ ID NO:263, b is an integer of 15 to 1654, where both a	AA193057, AA459842

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:263, and where b is greater than or equal to a + 14.	
828573	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1154 of SEQ ID NO:264, b is an integer of 15 to 1168, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:264, and where b is greater than or equal to a + 14.	W21349, AA287428, AA488879, AA736676, AA825689, AA831957
828624	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1743 of SEQ ID NO:265, b is an integer of 15 to 1757, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:265, and where b is greater than or equal to a + 14.	T80978, T80979, R63642, R63643, H50751, AA130349, AA130348, AA228511, AA229376, AA558367, AA588171, AA602572, AA902186, AA907305
828656	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 400 of SEQ ID NO:266, b is an integer of 15 to 414, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:266, and where b is greater than or equal to a + 14.	
828848	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1438 of SEQ ID NO:267, b is an integer of 15 to 1452, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:267, and where b is greater than or equal to a + 14.	W74302, C06154
828929	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3045 of SEQ ID NO:268, b is an integer of 15 to 3059, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:268, and where b is greater than or equal to a + 14.	T71649, T66629, T82072, R16043, R18568, R25675, R27534, R37452, R37893, R49608, R49608, H00371, H04032, H15066, H15067, H17442, H25765, H25806, H42041, H42082, H98813, N21069, N26797, N27904, N30299, N32783, N35448, N39486, N41546, N42023, N47272, N48586, N51988, N53717, N62255, N72265, N95532, N95535, W02978, W24224, W24221, W37457, W49675, W49769, W94843, AA011118, AA017107, AA026474, AA026566, AA043220, AA053225, AA059038, AA127381, AA135518, AA135579, AA160002, AA161212, AA250957, AA251069, AA256560
829008	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 750 of SEQ ID NO:269, b is an integer of 15 to 764, where both a	

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:269, and where b is greater than or equal to $a + 14$.	
829086	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 518 of SEQ ID NO:270, b is an integer of 15 to 532, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:270, and where b is greater than or equal to $a + 14$.	
829192	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1383 of SEQ ID NO:271, b is an integer of 15 to 1397, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:271, and where b is greater than or equal to $a + 14$.	R01014, R18033, R68910, R99809, H52663, N58651, AA088731, AA193513, AA193662
829310	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 513 of SEQ ID NO:272, b is an integer of 15 to 527, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:272, and where b is greater than or equal to $a + 14$.	AA083295
829319	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 791 of SEQ ID NO:273, b is an integer of 15 to 805, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:273, and where b is greater than or equal to $a + 14$.	T90645, T90659, T97985, H06506, H19818, H20153, H20246, H21116, H21159, H21858, H41323, H41571, H42403, H42408, H42409, H42924, H42925, H44900, H46556, H50437, H50438, AA099620, AA102013, AA148703, AA148704
829459	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1939 of SEQ ID NO:274, b is an integer of 15 to 1953, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:274, and where b is greater than or equal to $a + 14$.	R09386, R09387, T78025, T97831, R23957, R23958, R24288, R24397, R26402, R28352, R28556, R28581, R63909, R63994, H02219, H04307, H04347, H06295, H06351, H13627, H13626, R84897, R85842, R98471, R98515, H72345, H81180, H95281, H95334, H99164, N29733, W03364, W47102, W47226, W92469, AA010223, AA011481, AA011482, AA016315, AA018837, AA101692, AA101805, AA101807, AA122274, AA121645, AA151559, AA149649, AA195694, AA195725, AA227519, AA232778, AA233860, AA234917, AA234918, AA253354, AA253355, AA258326, AA258535
829527	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2362 of SEQ ID NO:275, b is an integer of 15 to 2376, where both a	T58131, T63068, T90761, T80172, T83210, T96126, T96208, R02011, R02010, R13993, R37587, R39116, R49772, H04979, H04978, H10390, H10599, H25348, R89064, R89161,

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:275, and where b is greater than or equal to $a + 14$.	W40553, W42765, W57719, W57718, AA125861, AA125860, AA187443, AA187617, AA234055, AA430020
829736	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2425 of SEQ ID NO:276, b is an integer of 15 to 2439, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:276, and where b is greater than or equal to $a + 14$.	T49267, T49268, T49304, T49305, T63879, T80451, T81311, T81839, T83362, T83508, T95341, T95436, R22333, R25604, R34248, R35407, R35574, R49204, R49204, R62803, R62852, H13144, H17521, H44982, R93505, R93504, H98806, N24673, N25026, N32953, N33048, N35464, N42110, N42625, N55468, N76843, W03837, AA056568, AA056719, AA150946, AA151038, AA165138, AA169548, AA169352, AA171757, AA171713, AA171996, AA172106, AA235604, AA424478
830552	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1875 of SEQ ID NO:277, b is an integer of 15 to 1889, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:277, and where b is greater than or equal to $a + 14$.	
830566	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 622 of SEQ ID NO:278, b is an integer of 15 to 636, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:278, and where b is greater than or equal to $a + 14$.	H58586
830568	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2847 of SEQ ID NO:279, b is an integer of 15 to 2861, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:279, and where b is greater than or equal to $a + 14$.	T86173, T86174, R31229, R56392, H27334, H41900, H41939, N41528, AA464551, AA464652, AA425346, AA430320, AA514778, AA551699, AA558620, AA558725, AA583577, AA612719, AA574033, AA746483, AA808281, AA831559, AA873069, AA878486, W22260, W22881, N88548, C04008, C04877, C05565
830569	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1492 of SEQ ID NO:280, b is an integer of 15 to 1506, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:280, and where b is greater than or equal to $a + 14$.	AA148863, AA148864
830583	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1679 of SEQ ID NO:281, b is an integer of 15 to 1693, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:281, and where b is	

	greater than or equal to $a + 14$.	
830613	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1209 of SEQ ID NO:282, b is an integer of 15 to 1223, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:282, and where b is greater than or equal to $a + 14$.	
830686	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 476 of SEQ ID NO:283, b is an integer of 15 to 490, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:283, and where b is greater than or equal to $a + 14$.	
830691	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2995 of SEQ ID NO:284, b is an integer of 15 to 3009, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:284, and where b is greater than or equal to $a + 14$.	T64847, T72590, R21403, R46500, R46500, R59229, R59289, H30531, H40605, H46249, H46370, H49841, H91758, AA125799, AA135387, AA135994, AA464935, AA424273, AA568294, AA810246, D80751, D81702, AA092153
830716	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 862 of SEQ ID NO:285, b is an integer of 15 to 876, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:285, and where b is greater than or equal to $a + 14$.	
830792	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 847 of SEQ ID NO:286, b is an integer of 15 to 861, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:286, and where b is greater than or equal to $a + 14$.	
830893	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1054 of SEQ ID NO:287, b is an integer of 15 to 1068, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:287, and where b is greater than or equal to $a + 14$.	
830976	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2242 of SEQ ID NO:288, b is an integer of 15 to 2256, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:288, and where b is greater than or equal to $a + 14$.	

831043	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 317 of SEQ ID NO:289, b is an integer of 15 to 331, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:289, and where b is greater than or equal to a + 14.	
831131	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 691 of SEQ ID NO:290, b is an integer of 15 to 705, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:290, and where b is greater than or equal to a + 14.	
831164	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 938 of SEQ ID NO:291, b is an integer of 15 to 952, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:291, and where b is greater than or equal to a + 14.	T74499, R12051, R18399, R60836, H15297, H18858, H23172, AA721309, AA831174, C04626
831173	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 590 of SEQ ID NO:292, b is an integer of 15 to 604, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:292, and where b is greater than or equal to a + 14.	
831255	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 496 of SEQ ID NO:293, b is an integer of 15 to 510, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:293, and where b is greater than or equal to a + 14.	
831327	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 831 of SEQ ID NO:294, b is an integer of 15 to 845, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:294, and where b is greater than or equal to a + 14.	W38432, W44821, W51893, W51781, W52725, W59978, W60116, AA588704, C05911, C05915
831493	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1032 of SEQ ID NO:295, b is an integer of 15 to 1046, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:295, and where b is greater than or equal to a + 14.	
831500	Preferably excluded from the present invention are	T67004, T67005, R06266, R06324,

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1902 of SEQ ID NO:296, b is an integer of 15 to 1916, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:296, and where b is greater than or equal to a + 14.	R55532, R55533, W60669, W60670, W96122, W96123, AA551364, AA553611, AA570432
831501	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1462 of SEQ ID NO:297, b is an integer of 15 to 1476, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:297, and where b is greater than or equal to a + 14.	R52091, H14837, AA023003, AA022470, AA232097, AA256032, AA258844, AA259023, AA424828, AA557330, AA765793
831502	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 527 of SEQ ID NO:298, b is an integer of 15 to 541, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:298, and where b is greater than or equal to a + 14.	
831508	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 457 of SEQ ID NO:299, b is an integer of 15 to 471, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:299, and where b is greater than or equal to a + 14.	
831509	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 928 of SEQ ID NO:300, b is an integer of 15 to 942, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:300, and where b is greater than or equal to a + 14.	
831520	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 447 of SEQ ID NO:301, b is an integer of 15 to 461, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:301, and where b is greater than or equal to a + 14.	
831547	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 892 of SEQ ID NO:302, b is an integer of 15 to 906, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:302, and where b is greater than or equal to a + 14.	R09826, T95977, T97888, H66377, W31141
831548	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide	T95880, T97781, R05685, R12413, R37130, R37412, R94523, H82826.

	sequence described by the general formula of a-b, where a is any integer between 1 to 606 of SEQ ID NO:303, b is an integer of 15 to 620, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:303, and where b is greater than or equal to a + 14.	H99806, H99813, AA172251, AA468699, AA659754, AA808925, AA837298, AA858110, AA864723, AA954263, F18115, N99864
831558	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 519 of SEQ ID NO:304, b is an integer of 15 to 533, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:304, and where b is greater than or equal to a + 14.	H60157, W57916, W57917, AA056029, AA056047, AA142858, AA211887, AA469104, AA659257, AA662867, AA665372, AA728846, AA933045, F17890, AA090265
831847	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1360 of SEQ ID NO:305, b is an integer of 15 to 1374, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:305, and where b is greater than or equal to a + 14.	
831893	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 654 of SEQ ID NO:306, b is an integer of 15 to 668, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:306, and where b is greater than or equal to a + 14.	
831903	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1032 of SEQ ID NO:307, b is an integer of 15 to 1046, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:307, and where b is greater than or equal to a + 14.	
831921	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1672 of SEQ ID NO:308, b is an integer of 15 to 1686, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:308, and where b is greater than or equal to a + 14.	H52554, H66743, H71667, N32238, N77727, W19857, AA017111, AA074918, AA235917, AA236708
831923	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1412 of SEQ ID NO:309, b is an integer of 15 to 1426, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:309, and where b is greater than or equal to a + 14.	
831959	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b,	

	where a is any integer between 1 to 1479 of SEQ ID NO:310, b is an integer of 15 to 1493, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:310, and where b is greater than or equal to a + 14.	
832008	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2328 of SEQ ID NO:311, b is an integer of 15 to 2342, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:311, and where b is greater than or equal to a + 14.	
832107	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 840 of SEQ ID NO:312, b is an integer of 15 to 854, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:312, and where b is greater than or equal to a + 14.	N38762, W81128, W81129
832110	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1487 of SEQ ID NO:313, b is an integer of 15 to 1501, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:313, and where b is greater than or equal to a + 14.	W72867, W76102, AA557708
832146	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1179 of SEQ ID NO:314, b is an integer of 15 to 1193, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:314, and where b is greater than or equal to a + 14.	
832189	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 784 of SEQ ID NO:315, b is an integer of 15 to 798, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:315, and where b is greater than or equal to a + 14.	AA004742, AA236306
832295	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1921 of SEQ ID NO:316, b is an integer of 15 to 1935, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:316, and where b is greater than or equal to a + 14.	H21746, H21943, H39580, AA455263, AA455264, AA465644, AA563903, AA576922, AA661801, AA747311, AA767674, AA933667, A1088750
832334	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1724 of SEQ ID	

	NO:317. b is an integer of 15 to 1738, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:317, and where b is greater than or equal to a + 14.	
832339	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1326 of SEQ ID NO:318. b is an integer of 15 to 1340, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:318, and where b is greater than or equal to a + 14.	
832393	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 770 of SEQ ID NO:319. b is an integer of 15 to 784, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:319, and where b is greater than or equal to a + 14.	
832415	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3513 of SEQ ID NO:320. b is an integer of 15 to 3527, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:320, and where b is greater than or equal to a + 14.	T65740, R78913, R79012, R82303, R82302, H13769, H81248, H81589, H88099, H95138, H97042, H81589, N21407, N25252, N29919, N31363, N33888, N42972, N50375, N51590, W38583, W69205, W69309, W73506, W73337, N90198, AA099534, AA099533, AA173671, AA173689, AA252476
832422	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1435 of SEQ ID NO:321. b is an integer of 15 to 1449, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:321, and where b is greater than or equal to a + 14.	T99380, T99603, N31610, N32587, N42671, N47813, AA009818, AA009819, AA166785, AA166950, AA507182, AA569843, D78758, C04932
832448	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 763 of SEQ ID NO:322. b is an integer of 15 to 777, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:322, and where b is greater than or equal to a + 14.	
832532	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1200 of SEQ ID NO:323. b is an integer of 15 to 1214, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:323, and where b is greater than or equal to a + 14.	
832621	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1032 of SEQ ID	W24985, W47319, AA922747

	NO:324, b is an integer of 15 to 1046, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:324, and where b is greater than or equal to a + 14.	
832622	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 660 of SEQ ID NO:325, b is an integer of 15 to 674, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:325, and where b is greater than or equal to a + 14.	
835327	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 343 of SEQ ID NO:326, b is an integer of 15 to 357, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:326, and where b is greater than or equal to a + 14.	
835695	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1565 of SEQ ID NO:327, b is an integer of 15 to 1579, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:327, and where b is greater than or equal to a + 14.	
835857	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2258 of SEQ ID NO:328, b is an integer of 15 to 2272, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:328, and where b is greater than or equal to a + 14.	
836183	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1306 of SEQ ID NO:329, b is an integer of 15 to 1320, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:329, and where b is greater than or equal to a + 14.	
836190	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1846 of SEQ ID NO:330, b is an integer of 15 to 1860, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:330, and where b is greater than or equal to a + 14.	
836196	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1562 of SEQ ID NO:331, b is an integer of 15 to 1576, where both a	T53851, T53923, R63103, R76448, R76703, N35338, N44709, N75001, N98466, N98613, N98769, W05702, W24237, W31023, W30985, W38813, W38941, W42920, W42850, W47106.

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:331, and where b is greater than or equal to a + 14.	W47230, W56833, W60274, W67278, W67414, N89826, AA043314, AA043313, AA046060, AA046186, AA102070, AA099937, AA502040, AA507883, AA507901, AA533422, AA847757, AA877285, AA878535, AA887648, AA970407, AA653954, AA291528
836253	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 562 of SEQ ID NO:332, b is an integer of 15 to 576, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:332, and where b is greater than or equal to a + 14.	
836372	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1297 of SEQ ID NO:333, b is an integer of 15 to 1311, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:333, and where b is greater than or equal to a + 14.	
837077	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1104 of SEQ ID NO:334, b is an integer of 15 to 1118, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:334, and where b is greater than or equal to a + 14.	AA604913, AA576835, AA862767, AA902805, A1080476
837445	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2252 of SEQ ID NO:335, b is an integer of 15 to 2266, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:335, and where b is greater than or equal to a + 14.	
837620	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1118 of SEQ ID NO:336, b is an integer of 15 to 1132, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:336, and where b is greater than or equal to a + 14.	
837981	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2215 of SEQ ID NO:337, b is an integer of 15 to 2229, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:337, and where b is greater than or equal to a + 14.	
837995	Preferably excluded from the present invention are	T51581, T68704, T68747, T68770.

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3714 of SEQ ID NO:338, b is an integer of 15 to 3728, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:338, and where b is greater than or equal to a + 14.	T68795, T68814, T73080, T73178, T73508, T83922, T87588, T78456, T78483, T78523, T78568, T79931, T83750, R16916, R16973, R73535, R73536, R95125, R95126, R99128, H48427, H65045, H65046, H65601, H72506, H72904, H73672, H73416, H75352, H79656, N55345, N69659, N77351, N94268, N94637, W19274, W23857, W24361, W42977, W48819, W68303, W68486, AA037188, AA044094, AA044284, AA055252, AA055253, AA186602, AA188281, AA177045, AA229943, AA514508, AA557392, AA565513, H80617, AA588181, AA635650, AA580469, AA687441, AA687497, AA834363, AA878670, AA906758, AA934579, AA948660, AA995311, C06397, AA284956, AA285113, AA292550
838001	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2660 of SEQ ID NO:339, b is an integer of 15 to 2674, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:339, and where b is greater than or equal to a + 14.	
838237	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1443 of SEQ ID NO:340, b is an integer of 15 to 1457, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:340, and where b is greater than or equal to a + 14.	
838700	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3385 of SEQ ID NO:341, b is an integer of 15 to 3399, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:341, and where b is greater than or equal to a + 14.	
838805	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1915 of SEQ ID NO:342, b is an integer of 15 to 1929, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:342, and where b is greater than or equal to a + 14.	
839096	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1547 of SEQ ID NO:343, b is an integer of 15 to 1561, where both a	

	and b correspond to the positions of nucleotide residues shown in SEQ ID NO:343, and where b is greater than or equal to a + 14.	
839185	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2968 of SEQ ID NO:344, b is an integer of 15 to 2982, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:344, and where b is greater than or equal to a + 14.	
839588	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1640 of SEQ ID NO:345, b is an integer of 15 to 1654, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:345, and where b is greater than or equal to a + 14.	
839589	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 484 of SEQ ID NO:346, b is an integer of 15 to 498, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:346, and where b is greater than or equal to a + 14.	
839733	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3162 of SEQ ID NO:347, b is an integer of 15 to 3176, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:347, and where b is greater than or equal to a + 14.	T49124, T49125, T87606, T80183, R17716, R25789, R37588, R41786, R46788, R41786, R46788, R86012, N27045, N27365, N31477, N75044, N80842, N92937, N99972, W05771, AA007622, AA007661, AA035367, AA135176, AA135350, AA458470, AA505865, AA506506, AA526375, AA613311, AA613813, AA636046, AA639686, AA569896, AA687824, AA740795, AA828494, AA830137, AA836424, AA902192, AA907444, AA910103, AA916663, AA961769, AA987257, AA995286, C02440, C03271, C04496, AA400614, AA401259, AA401972, AA402117, AA404233, AA442982, AA453509, AA453510, AA454684, AA456333, AA845142, AA854089, AA813552, AA860919, A1024368, A1078067, D30835, D31579
839874	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1113 of SEQ ID NO:348, b is an integer of 15 to 1127, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:348, and where b is greater than or equal to a + 14.	H11826, H19387, AA082620
840017	Preferably excluded from the present invention are	

	one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2121 of SEQ ID NO:349, b is an integer of 15 to 2135, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:349, and where b is greater than or equal to a + 14.	
840124	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1564 of SEQ ID NO:350, b is an integer of 15 to 1578, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:350, and where b is greater than or equal to a + 14.	
840222	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 960 of SEQ ID NO:351, b is an integer of 15 to 974, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:351, and where b is greater than or equal to a + 14.	R84486, R84529, R88248, Z43097
840617	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2587 of SEQ ID NO:352, b is an integer of 15 to 2601, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:352, and where b is greater than or equal to a + 14.	
840641	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 907 of SEQ ID NO:353, b is an integer of 15 to 921, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:353, and where b is greater than or equal to a + 14.	H50311, N31637, N38837, N57092, W25229, W35251, W58039, W58123, W72521, W76080, N89999, AA256075, AA256114, AA426416, AA279475, AA287965, AA286961, AA286962, AA405003, AA521338, AA588308, AA729660, AA732508, AA736855, AA760789, AA765636, AA766365, AA805546, AA825927, AA911323, AA917840, AA918945, AA922719, AA939023, AA969474, AA976724, N95393, AA453687, AA482391, AA447756, AA706719, AA709036, AA719892, A1089099, D20399
840792	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1297 of SEQ ID NO:354, b is an integer of 15 to 1311, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:354, and where b is greater than or equal to a + 14.	R23893, R23892, R32223, R81610, H00321, N30960, N66394, W40278, W40275, W45359, W56625, W56539, AA025789, AA025949, AA126511, AA126636, AA131184, AA131120, AA131260, AA135445, AA164894, AA164893, AA181943, AA262234, AA460727, AA460899, AA614654, AA576166, AA577101, AA577111, AA814470, AA962227, AA996044, C00083, C18672, AA644060, AA635144, AA725839, AA960853,

		AA992056, AI003313, AI014315, AI024320, AI122746, T24622
840915	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2239 of SEQ ID NO:355, b is an integer of 15 to 2253, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:355, and where b is greater than or equal to a + 14.	
841059	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1221 of SEQ ID NO:356, b is an integer of 15 to 1235, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:356, and where b is greater than or equal to a + 14.	
841325	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1394 of SEQ ID NO:357, b is an integer of 15 to 1408, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:357, and where b is greater than or equal to a + 14.	R28417, R28429, AA279887, AA481504
841713	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 858 of SEQ ID NO:358, b is an integer of 15 to 872, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:358, and where b is greater than or equal to a + 14.	
842324	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1730 of SEQ ID NO:359, b is an integer of 15 to 1744, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:359, and where b is greater than or equal to a + 14.	
842386	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 659 of SEQ ID NO:360, b is an integer of 15 to 673, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:360, and where b is greater than or equal to a + 14.	
842454	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1310 of SEQ ID NO:361, b is an integer of 15 to 1324, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:361, and where b is	

	greater than or equal to $a + 14$.	
842768	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 664 of SEQ ID NO:362, b is an integer of 15 to 678, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:362, and where b is greater than or equal to $a + 14$.	
842999	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 5222 of SEQ ID NO:363, b is an integer of 15 to 5236, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:363, and where b is greater than or equal to $a + 14$.	
843830	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1006 of SEQ ID NO:364, b is an integer of 15 to 1020, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:364, and where b is greater than or equal to $a + 14$.	
844723	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2194 of SEQ ID NO:365, b is an integer of 15 to 2208, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:365, and where b is greater than or equal to $a + 14$.	
844868	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2741 of SEQ ID NO:366, b is an integer of 15 to 2755, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:366, and where b is greater than or equal to $a + 14$.	
845258	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1950 of SEQ ID NO:367, b is an integer of 15 to 1964, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:367, and where b is greater than or equal to $a + 14$.	R24215, R24216, R66047, R66048, H02011, H12618, H12668, H90748, H90799, N69833, N93931, N98972, W40431, W90007, AA024872, AA115390, AA133417, AA194946, AA195087, AA195556, AA195715, AA195752, AA425375, AA425467, AA903701, A1078393, Z44587, AA700297, AA702853
845373	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3033 of SEQ ID NO:368, b is an integer of 15 to 3047, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:368, and where b is	

	greater than or equal to $a + 14$.	
845412	Preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2397 of SEQ ID NO:369, b is an integer of 15 to 2411, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:369, and where b is greater than or equal to $a + 14$.	

Polynucleotide and Polypeptide Variants

The present invention is directed to variants of the polynucleotide sequence disclosed in SEQ ID NO:X or the complementary strand thereto, and/or the cDNA sequence contained in a cDNA clone contained in the deposit.

5 The present invention also encompasses variants of the pancreas and pancreatic cancer polypeptide sequence disclosed in SEQ ID NO:Y, a polypeptide sequence encoded by the polynucleotide sequence in SEQ ID NO:X, and/or a polypeptide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

10 "Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

 The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%,
15 97%, 98%, 99% or 100%, identical to, for example, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence of the related cDNA contained in a deposited library or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a nucleotide
20 sequence encoding the polypeptide encoded by the cDNA in the related cDNA contained in a deposited library, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polypeptides encoded by these nucleic acid molecules are also encompassed by the invention. In another embodiment, the invention encompasses nucleic acid molecules which comprise or alternatively consist of,
25 a polynucleotide which hybridizes under stringent hybridization conditions, or alternatively, under low stringency conditions, to the nucleotide coding sequence in SEQ ID NO:X, the nucleotide coding sequence of the related cDNA clone contained in a deposited library, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a
30 nucleotide sequence encoding the polypeptide encoded by the cDNA in the related cDNA clone contained in a deposited library, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which

hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

The present invention is also directed to polypeptides which comprise, or alternatively
5 consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to, for example, the polypeptide sequence shown in SEQ ID NO:Y, a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the cDNA in the related cDNA clone contained in a deposited library, and/or polypeptide fragments of any of these polypeptides (e.g., those fragments described
10 herein). Polynucleotides which hybridize to the complement of the nucleic acid molecules encoding these polypeptides under stringent hybridization conditions, or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical"
15 to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to
20 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be, for example, an entire sequence referred to in Table 1, an ORF (open reading frame), or any fragment specified as described herein.

25 As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global
30 sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be

compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size
5 Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the
10 subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment.
15 This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of
20 manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and
25 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which
30 are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other

manual corrections are to made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that
5 the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur
10 at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence in SEQ ID
15 NO:Y or a fragment thereof, the amino acid sequence encoded by the nucleotide sequence in SEQ ID NO:X or a fragment thereof, or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library, or a fragment thereof, can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present
20 invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci.6:237- 245(1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a
25 FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal
30 deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences

truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C- terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which less than 50, less

than 40, less than 30, less than 20, less than 10, or 5-50, 5-25, 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, as discussed herein, one or more amino acids can be deleted from the N-terminus or C-terminus of the polypeptide of the present invention without substantial loss of biological function. The authors of Ron et al., *J. Biol. Chem.* 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., *J. Biotechnology* 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (*J. Biol. Chem.* 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, as discussed herein, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more

biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

Thus, the invention further includes polypeptide variants which show a functional activity (e.g., biological activity) of the polypeptide of the invention of which they are a variant. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as to have little effect on activity.

The present application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein or fragments thereof, (e.g., including but not limited to fragments encoding a polypeptide having the amino acid sequence of an N and/or C terminal deletion), irrespective of whether they encode a polypeptide having functional activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having functional activity include, inter alia, (1) isolating a gene or allelic or splice variants thereof in a cDNA library; (2) in situ hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the gene, as described in Verma et al., Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York (1988); and (3) Northern Blot analysis for detecting mRNA expression in specific tissues.

Preferred, however, are nucleic acid molecules having sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, which do, in fact, encode a polypeptide having a functional activity of a polypeptide of the invention.

Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to, for example, the nucleic acid sequence of the cDNA in the related cDNA clone contained in a

deposited library, the nucleic acid sequence referred to in Table 1 (SEQ ID NO:X), or fragments thereof, will encode polypeptides "having functional activity." In fact, since degenerate variants of any of these nucleotide sequences all encode the same polypeptide, in many instances, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.

For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," *Science* 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, *Science* 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side

chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly. Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

A further embodiment of the invention relates to a polypeptide which comprises the amino acid sequence of a polypeptide having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions. Of course it is highly preferable for a polypeptide to have an amino acid sequence which comprises the amino acid sequence of a polypeptide of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, and/or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library which contains, in order of ever-increasing preference, at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1

amino acid substitutions. In specific embodiments, the number of additions, substitutions, and/or deletions in the amino acid sequence of SEQ ID NO:Y or fragments thereof (e.g., the mature form and/or other fragments described herein), an amino acid sequence encoded by SEQ ID NO:X or fragments thereof, and/or the amino acid sequence encoded by the cDNA in the related cDNA clone contained in a deposited library or fragments thereof, is 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, conservative amino acid substitutions are preferable.

Polynucleotide and Polypeptide Fragments

The present invention is also directed to polynucleotide fragments of the pancreas and pancreatic cancer polynucleotides (nucleic acids) of the invention. In the present invention, a "polynucleotide fragment" refers, for example, to a polynucleotide having a nucleic acid sequence which: is a portion of the cDNA contained in a deposited cDNA clone; or is a portion of a polynucleotide sequence encoding the polypeptide encoded by the cDNA contained in a deposited cDNA clone; or is a portion of the polynucleotide sequence in SEQ ID NO:X or the complementary strand thereto; or is a polynucleotide sequence encoding a portion of the polypeptide of SEQ ID NO:Y; or is a polynucleotide sequence encoding a portion of a polypeptide encoded by SEQ ID NO:X or the complementary strand thereto. The nucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, at least about 100 nt, at least about 125 nt or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from, for example, the sequence contained in the cDNA in a related cDNA clone contained in a deposited library, the nucleotide sequence shown in SEQ ID NO:X or the complementary stand thereto. In this context "about" includes the particularly recited value or a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., at least 150, 175, 200, 250, 500, 600, 1000, or 2000 nucleotides in length) are also encompassed by the invention.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-

400, 401-450, 451-500, 501-550, 551-600, 651-700, 701- 750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, and 3551 to the end of SEQ ID NO:X, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity) of the polypeptide encoded by the polynucleotide of which the sequence is a portion. More preferably, these fragments can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides or fragments.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701- 750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, and 3551 to the end of the cDNA nucleotide sequence contained in the deposited cDNA clone, or the complementary strand thereto. In this context "about" includes the particularly recited range, or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a

functional activity (e.g., biological activity) of the polypeptide encoded by the cDNA nucleotide sequence contained in the deposited cDNA clone. More preferably, these fragments can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these fragments under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides or fragments.

In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y, a portion of an amino acid sequence encoded by the polynucleotide sequence of SEQ ID NO:X, and/or encoded by the cDNA contained in the related cDNA clone contained in a deposited library. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, an amino acid sequence from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, and 1181 to the end of SEQ ID NO:Y. Moreover, polypeptide fragments of the invention may be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, or ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either terminus or at both termini. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

Even if deletion of one or more amino acids from the N-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example, the ability of shortened muteins to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptides generally will be retained

when less than the majority of the residues of the complete or mature polypeptide are removed from the N-terminus. Whether a particular polypeptide lacking N-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a
5 mutein with a large number of deleted N-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

Accordingly, polypeptide fragments of the invention include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein
10 or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above
15 amino and carboxy terminus deletions are preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

The present invention further provides polypeptides having one or more residues deleted from the amino terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide
20 sequence contained in SEQ ID NO:X, and/or a polypeptide encoded by the cDNA contained in the related cDNA clone contained in a deposited library). In particular, N-terminal deletions may be described by the general formula m-q, where q is a whole integer representing the total number of amino acid residues in a polypeptide of the invention (e.g., the polypeptide disclosed in SEQ ID NO:Y), and m is defined as any integer ranging from 2
25 to q-6. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example the ability of the shortened mutein
30 to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular

polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides
5 composed of as few as six amino acid residues may often evoke an immune response.

Accordingly, the present invention further provides polypeptides having one or more residues from the carboxy terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, and/or a polypeptide encoded by the cDNA contained
10 in deposited cDNA clone referenced in Table 1). In particular, C-terminal deletions may be described by the general formula 1-n, where n is any whole integer ranging from 6 to q-1, and where n corresponds to the position of an amino acid residue in a polypeptide of the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

15 In addition, any of the above described N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of a polypeptide encoded by SEQ ID NO:X (e.g., including, but not limited to, the preferred polypeptide disclosed as SEQ ID
20 NO:Y), and/or the cDNA in the related cDNA clone contained in a deposited library, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Any polypeptide sequence contained in the polypeptide of SEQ ID NO:Y, encoded by the polynucleotide sequences set forth as SEQ ID NO:X, or encoded by the cDNA in the
25 related cDNA clone contained in a deposited library may be analyzed to determine certain preferred regions of the polypeptide. For example, the amino acid sequence of a polypeptide encoded by a polynucleotide sequence of SEQ ID NO:X, or the cDNA in a deposited cDNA clone may be analyzed using the default parameters of the DNASTAR computer algorithm (DNASTAR, Inc., 1228 S. Park St., Madison, WI 53715 USA; <http://www.dnastar.com/>).

30 Polypeptide regions that may be routinely obtained using the DNASTAR computer algorithm include, but are not limited to, Garnier-Robson alpha-regions, beta-regions, turn-regions, and coil-regions, Chou-Fasman alpha-regions, beta-regions, and turn-regions,

Kyte-Doolittle hydrophilic regions and hydrophobic regions, Eisenberg alpha- and beta-amphipathic regions, Karplus-Schulz flexible regions, Emini surface-forming regions and Jameson-Wolf regions of high antigenic index. Among highly preferred polynucleotides of the invention in this regard are those that encode polypeptides comprising regions that combine several structural features, such as several (e.g., 1, 2, 3 or 4) of the features set out above.

Additionally, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Emini surface-forming regions, and Jameson-Wolf regions of high antigenic index (i.e., containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) can routinely be used to determine polypeptide regions that exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from data by DNASTAR analysis by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

Preferred polypeptide fragments of the invention are fragments comprising, or alternatively consisting of, an amino acid sequence that displays a functional activity of the polypeptide sequence of which the amino acid sequence is a fragment.

By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

In preferred embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the antigenic fragments of the polypeptide of

SEQ ID NO:Y, or portions thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Table 4.

Sequence/ Contig ID	Epitope
462108	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 461 as residues: Ile-1 to Arg-9, Val-26 to Val-41, Met-46 to Cys-51, Trp-88 to Gln-93, Glu-124 to Trp-130, Gly-339 to Pro-344.
503446	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 462 as residues: Leu-54 to Leu-60.
507841	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 463 as residues: Tyr-39 to Trp-44.
509287	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 464 as residues: Arg-6 to Val-12, Thr-38 to Asn-43, Arg-69 to Asp-74, Trp-87 to Lys-97, His-136 to Met-142, Ala-149 to Lys-160.
509672	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 465 as residues: Ser-33 to Cys-39.
524112	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 469 as residues: Asp-1 to Gly-6, Pro-30 to Gly-40, Leu-46 to Asn-52, Asp-54 to Gly-61.
525971	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 470 as residues: Pro-13 to Arg-21, Leu-30 to Thr-35, Pro-43 to Ser-51.
527156	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 471 as residues: Ala-2 to Pro-7.
532502	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 472 as residues: Lys-1 to Ser-6.
533459	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 473 as residues: Gly-1 to Trp-7, Ile-155 to Gly-163.
533551	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 474 as residues: Lys-15 to Leu-20.
537850	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 475 as residues: Ile-43 to Leu-49, Cys-85 to Lys-92, Phe-138 to Leu-144.
537925	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 476 as residues: Gln-17 to Ser-24, Ala-47 to Asn-52.
540802	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 479 as residues: Leu-3 to Trp-9, Arg-20 to Phe-29, Glu-58 to Gln-65.
540989	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 480 as residues: Ser-52 to Gly-57, Thr-64 to Asn-70.
540997	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 481 as residues: Ile-1 to Thr-11.
548735	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 482 as residues: Gln-17 to Asn-22, Ser-38 to Pro-45, Asn-75 to Leu-84, Glu-97 to Pro-110.
549709	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 483 as residues: Phe-65 to Trp-77.
550007	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 484 as residues: Ser-4 to Ser-13, Leu-22 to Cys-40, Gly-42 to Gly-50, Thr-88 to Glu-97, Leu-184 to Gln-190, Pro-206 to Gly-211.
550118	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 485 as residues: Gly-1 to Gly-7, Trp-10 to Met-24, Gln-91 to Gly-98.
550870	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 487 as residues: Arg-26 to Arg-33, Gln-47 to Asn-52, Trp-61 to Ser-71, Gly-93 to Trp-100.
553765	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 489 as residues: Thr-8 to Thr-19, Arg-108 to Ser-115, Ser-117 to Arg-128, Phe-143 to Tyr-155, Leu-171 to Arg-177, Asn-182 to Gly-187, Gly-195 to Ser-200, Arg-232 to Thr-

	248, Pro-287 to Arg-293.
554050	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 490 as residues: Asp-49 to Lys-54, Glu-80 to Glu-86, Lys-121 to Leu-126, Thr-160 to Val-165, Ile-176 to Gly-181.
554186	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 491 as residues: Gln-1 to Cys-6, Asn-17 to Ala-24, Ala-157 to Asp-162, Ser-180 to Asp-185, Leu-219 to Thr-227, Lys-239 to Ile-246, Pro-266 to Asp-271.
554716	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 492 as residues: Thr-2 to His-10, Ser-51 to Ser-58, Ile-84 to Lys-89.
556791	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 493 as residues: Asp-31 to Lys-37, Ser-58 to Phe-63, Lys-70 to Thr-79, Asp-100 to Ile-108.
557121	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 494 as residues: Leu-29 to Gly-35, Ser-39 to Ala-47, Gln-91 to Arg-107.
557199	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 495 as residues: Ser-2 to His-12, Ser-14 to Ser-24, Gly-47 to Tyr-52, Pro-115 to Gly-126.
557293	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 496 as residues: Pro-14 to Gly-21, Pro-25 to Gly-36, Ala-43 to Gly-48, Pro-53 to Gly-78, Arg-90 to Asp-96, Pro-98 to Gly-103, Gln-117 to His-123, Ala-154 to Tyr-161.
558423	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 499 as residues: Gln-43 to Ile-49, Ala-106 to His-113, Glu-151 to Lys-156, Ala-186 to Arg-191, Lys-212 to Leu-223.
558465	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 500 as residues: Arg-1 to Arg-7, Gln-14 to Glu-22, Lys-52 to Gln-57, Lys-89 to Gly-96, Gly-103 to Ser-112, Ser-153 to His-168.
558778	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 502 as residues: His-2 to Ser-18.
558818	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 503 as residues: Asp-1 to His-9.
572571	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 505 as residues: Ser-1 to Pro-6, His-26 to Gly-31, Pro-36 to Lys-42, Pro-65 to Val-71.
575525	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 506 as residues: Arg-10 to Pro-19, Thr-34 to Gly-44.
580659	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 507 as residues: Val-17 to Ile-24.
583650	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 508 as residues: Ser-10 to Pro-19, Pro-26 to Ala-31.
585791	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 510 as residues: Ser-40 to Tyr-50, Pro-95 to Thr-125, Lys-131 to Ile-142, Thr-165 to Arg-178.
587229	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 511 as residues: Glu-51 to Gly-56, Cys-75 to Lys-87, Pro-98 to Cys-107, Ser-115 to Glu-120, Ala-139 to Gln-155.
587246	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 512 as residues: Glu-1 to Val-9, Pro-66 to Thr-73, Phe-84 to Trp-93.
592154	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 515 as residues: Pro-17 to Tyr-28, Arg-62 to Cys-68, Lys-75 to Thr-87.
598665	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 517 as residues: Leu-102 to Gln-108, Ser-114 to Asn-123, Asn-155 to Arg-160, Thr-169 to Pro-175, Ile-201 to Gln-207, Ser-236 to Ala-249, Asp-257 to Trp-262, Pro-275 to Gly-282, Pro-320 to Gln-336, Leu-386 to Arg-391.
604719	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 518 as residues: Pro-14 to Cys-25, Val-104 to Ile-110, His-116 to Gln-122, Ser-130 to Glu-142, Asn-162 to Asn-168, Arg-185 to Ile-191, Ser-210 to Lys-217.

612689	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 519 as residues: Lys-22 to Thr-29, Asp-39 to Ala-44, Arg-60 to Ser-65.
612980	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 520 as residues: Leu-37 to Glv-44.
615134	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 521 as residues: His-23 to Gly-33, Cys-89 to Arg-95, Asn-127 to Ala-136, Arg-177 to Gln-183.
616064	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 522 as residues: Trp-7 to Ser-14, Cys-69 to Glu-80.
616096	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 523 as residues: Pro-11 to Arg-34.
616926	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 524 as residues: Arg-25 to His-39.
634923	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 525 as residues: Tyr-20 to Ser-26, Ser-48 to Asn-54.
647531	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 527 as residues: Asp-24 to Phe-30.
647699	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 529 as residues: Glu-85 to Glu-93, Pro-107 to Asn-116, Gln-185 to His-192.
651706	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 530 as residues: Ser-41 to Gly-47, Gln-63 to Val-71, Tyr-83 to Pro-90, Leu-123 to Ser-128, Pro-185 to Arg-190, Asp-203 to Asn-210, Lys-232 to Trp-237, Glu-243 to Ser-249, Gly-281 to Asn-289, Thr-306 to Glv-311.
654015	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 533 as residues: Phe-14 to Tyr-19.
657859	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 536 as residues: His-1 to Trp-10, Pro-12 to Ser-24.
662212	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 538 as residues: Pro-20 to Thr-47, Ser-54 to Pro-61.
662496	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 540 as residues: Thr-51 to Gly-63, Arg-65 to Phe-72, Phe-78 to Asp-86, Ser-89 to Gly-104.
670453	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 542 as residues: His-9 to Gln-14, Ile-112 to Gly-118, Arg-150 to Leu-157, His-187 to Gly-197, Pro-229 to Trp-235.
675028	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 543 as residues: Arg-1 to His-9, Asn-35 to Arg-40.
681325	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 544 as residues: Pro-15 to Arg-23.
683103	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 545 as residues: Arg-1 to Ser-7, Ser-37 to Gln-43, Pro-107 to Thr-119, His-146 to Asn-151, Glv-158 to Gln-177, Glu-201 to Lys-206, Thr-236 to Leu-242, Gly-265 to Arg-271.
684432	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 546 as residues: Asp-1 to Asn-7, Thr-72 to Gly-79, Val-94 to Gly-99, Arg-182 to Ala-191, Asn-203 to Ser-212.
688018	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 547 as residues: Glu-1 to Trp-11.
691522	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 549 as residues: Tyr-38 to Gly-45, Lys-102 to Leu-109, Lys-114 to Ser-119, Asp-161 to Gln-166, Gln-179 to Gly-188.
693706	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 550 as residues: Leu-57 to Phe-62, Leu-100 to Ser-105, Ile-119 to Pro-134, Asn-154 to Asn-165, Asp-173 to Lys-186, Leu-213 to Gly-222, Lys-225 to Glu-231, Asp-243 to Glu-248, Gln-307 to Lys-315, Glu-317 to Tyr-323, His-327 to Lys-334, Pro-362 to Arg-

	367. Lys-402 to Thr-409. Lys-446 to Glu-457. Arg-577 to Asn-587. Ser-619 to Arg-624. Ser-640 to Gly-646. Glu-654 to Gly-660. Pro-669 to Glu-674. Asn-694 to Lys-701. Ala-712 to Glu-725. His-749 to Asp-757.
694523	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 551 as residues: Thr-2 to Arg-9. Arg-17 to Glu-33.
697517	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 552 as residues: Val-21 to Leu-27. Glu-30 to His-36.
699054	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 553 as residues: Gln-1 to Gln-17. Leu-24 to Gly-36.
703402	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 555 as residues: Arg-47 to Arg-57. Gln-59 to Tyr-65. Pro-67 to Phe-75. Arg-92 to Phe-97. Glu-108 to Val-120.
703651	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 556 as residues: Lys-41 to His-51. Asp-65 to Lys-73.
704905	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 557 as residues: Pro-19 to Thr-27. Ala-63 to Ser-71. Leu-92 to Ala-97.
708515	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 559 as residues: Lys-25 to Gly-35. Pro-37 to Met-42. Glu-110 to Glu-119. Leu-123 to Gly-128.
710572	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 560 as residues: Trp-1 to Glu-8. Glu-14 to Met-24. Ala-38 to Val-50. Gly-72 to Leu-79.
710618	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 561 as residues: Lys-61 to Asp-66.
711810	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 562 as residues: Arg-1 to Ile-8. Pro-50 to Thr-62.
714933	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 563 as residues: Asp-59 to Ser-71. Asp-86 to Leu-99. Arg-118 to Tyr-123.
716331	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 564 as residues: Met-3 to Ser-9. Leu-86 to Ser-91.
717686	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 565 as residues: Arg-18 to Asn-25.
718187	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 566 as residues: Phe-24 to Lys-29.
719934	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 567 as residues: Ser-36 to Trp-41. Ser-55 to Asn-60. Thr-67 to Phe-74. Ser-87 to Thr-95. Lys-132 to Gln-144. Ala-186 to Gly-192. Pro-260 to Asn-265. Leu-289 to Tyr-295. Ala-336 to Gly-347. Gly-386 to Gln-393. Thr-400 to Ser-413.
722980	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 568 as residues: Arg-1 to Gly-9. Ala-54 to Asp-59.
723596	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 569 as residues: Glu-65 to Tyr-70.
724352	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 570 as residues: Val-6 to Asn-20. His-45 to Pro-56.
724904	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 573 as residues: Glu-4 to Leu-14. Arg-52 to Lys-58. Asp-60 to Ile-70. Val-85 to Asp-92. Pro-99 to Arg-111.
725642	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 574 as residues: Arg-1 to Thr-14. Pro-28 to Asp-33. Lys-92 to Leu-101.
726192	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 575 as residues: Val-7 to Ser-15.
730930	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 577 as residues: Phe-12 to Thr-18. Leu-30 to Leu-36. Thr-56 to Ser-62. Ile-115 to Phe-120.
732386	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 579 as

	residues: Thr-1 to Leu-12, Gly-39 to Gln-44, Thr-52 to Pro-59, Ser-88 to Pro-95, Val-122 to Gln-132, Asp-139 to Glu-144, Ser-177 to Ala-182, Gln-200 to Glv-207.
732909	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 580 as residues: Glu-45 to Arg-51, Pro-107 to Lys-115.
733088	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 581 as residues: Phe-6 to Pro-13, Glu-24 to Asn-32, Arg-58 to Asn-64, Arg-87 to Ile-95.
734760	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 584 as residues: Glu-1 to Trp-13, Gln-15 to Asp-22.
735711	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 585 as residues: Gln-11 to His-19, Val-30 to Ile-36, Pro-63 to Ser-69, Gly-78 to Ser-83, Ser-92 to Tyr-97, Gln-155 to Glu-161, Glv-237 to Thr-244.
742413	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 586 as residues: Gly-47 to Tyr-52, Thr-56 to Leu-62, Ser-65 to Thr-76, Leu-103 to Asp-144, Lys-149 to Leu-154, Asn-190 to Ser-198.
742676	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 587 as residues: Asn-2 to Ala-7.
742781	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 588 as residues: Thr-40 to Val-45, Lys-59 to Ser-64.
743356	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 589 as residues: Glv-4 to Lys-10.
750986	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 592 as residues: Arg-1 to Lys-7, Asn-20 to Gln-27, Phe-49 to Asn-58, Glu-63 to Gln-69, Gln-73 to Thr-78, Gln-136 to Leu-141, Ala-145 to Lys-153.
751068	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 593 as residues: Thr-5 to Ser-11.
751164	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 594 as residues: Gly-24 to Glv-32.
751890	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 595 as residues: Ala-24 to Ser-29.
751991	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 596 as residues: Tyr-1 to Gly-21, Ala-23 to Thr-29.
752449	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 597 as residues: Ser-17 to Thr-25.
752504	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 598 as residues: Arg-11 to Pro-26, Ala-37 to Asp-45, Asp-51 to Val-59, Glu-80 to Asp-98, Pro-104 to Trp-112, Asp-114 to Phe-124, Pro-140 to Pro-147, Pro-153 to Ala-158.
752688	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 599 as residues: Gly-1 to Pro-9, Arg-26 to Asp-31, Asp-33 to Val-58, Pro-71 to Ala-77, Ser-87 to Glv-95.
752889	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 600 as residues: Thr-1 to Lys-10.
753150	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 601 as residues: His-16 to Glu-35, Leu-43 to Tyr-55, His-68 to Gly-75, Ser-83 to Leu-89, Glu-106 to Ser-248, Ser-250 to Glu-306.
754479	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 603 as residues: Leu-47 to Ala-52, Ser-60 to Arg-80.
757127	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 606 as residues: Thr-25 to Ser-36.
757495	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 608 as residues: Arg-1 to Asp-6, Gln-46 to Val-59, Arg-93 to Ser-101, Gln-103 to Val-111, Pro-114 to Ser-119, Arg-138 to Glu-144, Ala-206 to Thr-212, Asn-228 to Asn-236, Asp-245 to Val-253, Pro-264 to Asp-270, His-295 to Asp-302, Leu-339 to Glu-349.
757715	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 609 as

	residues: Pro-1 to Val-15, Phe-21 to Val-27.
760388	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 610 as residues: Thr-24 to Gln-29, Val-56 to Gly-61.
760433	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 611 as residues: Thr-17 to Gln-33, Pro-35 to Arg-46, Ser-51 to Ala-58, Ser-98 to Leu-104, Phe-126 to Gly-137, Arg-139 to Leu-144, Ser-147 to Glu-153, Ala-164 to Gly-172.
760545	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 612 as residues: Met-1 to Phe-6.
761566	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 613 as residues: Glu-38 to Gly-43.
761740	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 614 as residues: Pro-35 to Asn-42, Lys-79 to Lys-84, Phe-131 to Cys-136.
766686	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 617 as residues: His-36 to Arg-48.
767396	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 618 as residues: Gln-33 to Asp-44, Pro-58 to Thr-79.
767501	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 619 as residues: Asp-1 to His-6, His-27 to Lys-37, Asn-141 to His-147, Asp-233 to Thr-239.
767945	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 620 as residues: Leu-5 to Leu-15.
771415	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 622 as residues: Gly-1 to Gly-9.
772657	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 623 as residues: Arg-1 to Gly-7, Gly-9 to Pro-21, Gly-39 to Arg-49, Thr-68 to Asn-73, Asp-78 to Arg-85, Thr-107 to Gln-116, Gln-147 to Arg-163, Gln-172 to Lys-187, Gln-240 to His-270, Tyr-282 to Ser-290.
773193	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 625 as residues: Gly-1 to Glu-13, Thr-29 to Ser-41, Gln-112 to His-123, Arg-133 to Gly-143.
773710	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 626 as residues: Ala-89 to Gly-94, Gly-108 to Thr-116, Leu-162 to Ala-167, Pro-169 to Ser-176, Val-217 to Arg-222.
774283	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 627 as residues: Asp-47 to Thr-71, Asp-78 to Ser-86, Pro-98 to Cys-103, Val-120 to Thr-129.
774369	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 628 as residues: Tyr-20 to Gly-26, Thr-36 to Ser-41, Lys-58 to Thr-64.
774754	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 629 as residues: Cys-5 to Glu-27, Glu-51 to Leu-75, Leu-86 to Phe-93, Val-169 to Lys-182, Ile-200 to Gln-206, Ala-250 to Met-257, Ser-301 to Asn-313, Asp-333 to Glu-342, Leu-344 to Asp-359, Asp-370 to Glu-381, Ser-390 to Gln-396.
774823	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 630 as residues: Leu-6 to Gln-12.
775510	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 631 as residues: Ser-15 to Ala-22.
775640	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 633 as residues: Ser-18 to Tyr-28.
775802	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 634 as residues: Val-1 to Glu-7.
777470	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 635 as residues: Arg-1 to Thr-11, Ala-45 to Glu-52, Cys-76 to Thr-88, Ala-94 to Arg-105, Asp-170 to Phe-178.

779273	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 638 as residues: Glu-46 to Phe-51, Pro-88 to Phe-95, Glv-104 to Val-110.
779297	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 639 as residues: Leu-25 to Arg-36, Ala-55 to Ser-60, Arg-67 to Tyr-84, Met-94 to Ala-100.
779664	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 640 as residues: Arg-34 to Ile-44, Ile-87 to Lys-108, Ile-128 to Met-139, Asp-143 to Gly-148.
781579	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 644 as residues: Gly-16 to Ser-37, Phe-83 to Asp-90.
782052	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 645 as residues: Arg-1 to Cys-12, Glu-15 to Pro-24.
782393	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 646 as residues: Tyr-1 to Glv-13, Glv-32 to Ser-39, Glu-71 to Ser-77.
782907	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 647 as residues: Ala-3 to Asp-22.
783220	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 648 as residues: Ser-8 to Leu-28, Asp-30 to Glu-43, Arg-48 to Pro-70, Glu-87 to Arg-97, Lys-106 to Pro-114.
783300	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 649 as residues: Thr-1 to Trp-15.
783938	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 650 as residues: Leu-13 to Arg-18, Lys-62 to Val-70, Phe-98 to Arg-107.
784024	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 651 as residues: Val-2 to Glu-7, Cys-15 to Tyr-32, Pro-52 to Arg-59.
784575	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 652 as residues: Asn-39 to His-44, Asp-59 to Met-64.
785006	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 653 as residues: Tyr-1 to Thr-10, Pro-12 to Pro-21.
785237	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 655 as residues: Glu-22 to Gln-29.
786111	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 656 as residues: Ala-1 to Thr-20, Cys-50 to Cys-63, Arg-70 to His-76, Pro-85 to Trp-93.
787036	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 657 as residues: Thr-31 to Gln-44, Ser-52 to Glu-57, Phe-73 to Ala-80, Thr-87 to Ser-94.
789626	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 660 as residues: Val-68 to Ser-74.
789703	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 661 as residues: Thr-8 to Lys-28, Cys-88 to Lys-96, Arg-98 to Ile-106, Asn-139 to Val-146, Glu-149 to Glu-162, Ser-172 to Arg-179, His-191 to Arg-196, Glu-214 to Leu-219, Glu-225 to Lys-260.
790848	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 663 as residues: Ser-47 to Lys-54.
790912	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 665 as residues: Gly-1 to Met-8, Arg-36 to Arg-43.
791386	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 666 as residues: Ser-20 to Gly-31, Phe-35 to Trp-45, Glu-52 to Trp-65, Thr-70 to Asp-78, Ala-86 to Glv-99, Glu-101 to Ala-106, Pro-112 to Trp-122.
791598	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 667 as residues: Arg-19 to Ala-30.
791619	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 668 as residues: Pro-39 to Asn-48, Ser-58 to Ile-69, Pro-72 to Gln-80, Ser-82 to Lys-103, Glu-111 to Pro-122, Ser-128 to Gln-157, Glu-172 to Ser-177.
791628	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 669 as

	residues: Ala-33 to Asp-39, Ala-81 to Ser-100.
791751	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 670 as residues: Arg-63 to Arg-72.
792557	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 671 as residues: Lys-51 to Arg-58.
792568	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 672 as residues: Glu-1 to Cys-9, Thr-65 to Leu-70, Asp-86 to Arg-92, Pro-132 to His-138.
793507	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 676 as residues: Pro-20 to Thr-25, Arg-60 to Asp-65.
793546	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 677 as residues: Pro-51 to Ser-56, Ser-62 to Thr-71, Leu-100 to Tyr-105, Pro-179 to Ala-186, Pro-200 to Lys-205, Glu-238 to Glu-243, Lys-250 to Tyr-261, Gln-317 to Gln-322.
793559	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 678 as residues: Glu-43 to Gln-48.
794121	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 680 as residues: Ala-1 to Glu-9, Gly-21 to Lys-29, Leu-31 to Lys-46, Pro-79 to Pro-85, Ser-111 to Leu-121, Arg-123 to Asn-138, Pro-146 to Arg-156.
794295	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 681 as residues: Arg-14 to Asp-21, Glu-29 to Ala-35, Thr-61 to Lys-66, Arg-91 to Gly-102, Ser-131 to Arg-144.
795241	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 682 as residues: Pro-5 to Asp-14, Pro-66 to Asn-74, Pro-83 to Asp-89, Glu-99 to His-104, Glu-116 to Ala-124, Leu-135 to Ala-142.
795286	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 683 as residues: Asn-13 to Thr-20.
795637	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 684 as residues: Phe-5 to Gly-17, His-68 to Glu-74, Pro-198 to Leu-203, Glu-205 to Lys-211, Val-245 to Trp-256, Phe-292 to Asn-297, Asp-325 to Gly-330, Gly-344 to Gln-360, Gly-379 to Gly-385, Glu-418 to Ser-427.
796301	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 685 as residues: Ala-4 to Asp-11, Ala-34 to Ser-43, Asp-50 to Ser-64, Arg-78 to Thr-95, Pro-104 to Ser-110, Ser-140 to Arg-148.
796590	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 688 as residues: Met-34 to Asp-42, Tyr-51 to Ala-56, Pro-67 to Leu-73, Ile-81 to Gly-88, Arg-166 to Val-172.
799783	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 689 as residues: Val-1 to Arg-9, Arg-26 to Gln-32, Arg-51 to Leu-63.
799784	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 690 as residues: Lys-19 to Arg-25, Phe-44 to Gln-49, Leu-70 to Ser-76.
799786	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 692 as residues: Thr-1 to Arg-19, Pro-22 to Arg-39, Pro-51 to Cys-78.
799800	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 694 as residues: Arg-8 to Ser-15, Thr-22 to Gly-43.
799808	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 695 as residues: Tyr-21 to Ser-26.
799977	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 696 as residues: Ser-28 to Ser-42.
800189	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 698 as residues: Arg-3 to Gln-14, Gln-18 to Gln-25, Lys-30 to Ser-36, Lys-75 to Thr-86, Glu-100 to Ser-107.
800589	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 699 as residues: Asp-1 to Asn-9, Lys-18 to Trp-31.

800811	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 700 as residues: Ser-1 to Leu-36, Leu-45 to Pro-78, Pro-80 to Thr-88, Leu-98 to Gly-123, Pro-126 to Ser-133, Asn-136 to Ser-149, Pro-160 to Gly-191.
805818	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 703 as residues: His-20 to Pro-25, Arg-72 to Ala-85, Pro-87 to His-102, Pro-128 to Arg-137, Met-145 to Leu-152, Arg-193 to Gly-199, Gly-269 to Arg-276, Pro-279 to Glu-284.
806579	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 705 as residues: Pro-54 to Ser-61, Leu-68 to Gln-74.
812314	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 709 as residues: Arg-1 to Gly-7, Leu-9 to Ser-16, Arg-25 to Cys-35.
812443	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 710 as residues: Lys-10 to Lys-24, Gln-30 to Glu-38, Thr-51 to Glu-62, Lys-85 to Tyr-90, Glu-171 to Trp-176, Glu-182 to Pro-188.
812498	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 711 as residues: Glu-57 to Ser-67.
813079	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 713 as residues: Asn-1 to Tyr-6, Met-24 to Asp-31, Glu-129 to Gly-135, Asp-164 to Lys-169.
815889	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 714 as residues: Lys-47 to Ile-64, Asp-72 to Glu-77, Lys-105 to Ala-111, Asp-145 to Gly-150, Asn-167 to Glu-172, Phe-180 to Gln-190.
824358	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 715 as residues: Ser-27 to Lys-32, Tyr-53 to Val-58, Lys-84 to Cys-89, Tyr-98 to Val-103, Asn-142 to Ser-156, Lys-162 to Glu-171, Ala-191 to Glu-231, Ala-237 to Tyr-247, Arg-254 to Thr-260, Tyr-267 to Ser-282.
826144	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 716 as residues: Ser-2 to Gly-7, Tyr-18 to Phe-26, Lys-39 to Gly-57, Gly-100 to Pro-106, Asn-109 to Ser-116, Tyr-119 to Ile-125, Pro-151 to Phe-157.
826558	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 717 as residues: Lys-4 to Ile-13, Arg-57 to His-62, Arg-68 to Gly-74.
827471	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 718 as residues: Lys-59 to Phe-69, Gln-98 to Thr-108, Pro-175 to Val-185, Asn-195 to Asp-206, Glu-214 to Gly-222, Ser-233 to Arg-240, Thr-258 to Thr-263, Pro-267 to Glu-272, Pro-278 to Glu-283, Pro-289 to Gly-294, Pro-300 to Gly-305, Pro-311 to Glu-316, Pro-322 to Gly-327, Pro-333 to Glu-338, Pro-344 to Ala-351.
827716	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 719 as residues: Lys-30 to Thr-37, Tyr-42 to Gly-54, Arg-93 to Thr-107, Pro-109 to Arg-116.
827722	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 720 as residues: Lys-1 to Lys-18.
827727	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 721 as residues: Lys-6 to Lys-24, Gln-50 to Glu-55, Arg-75 to Arg-90.
828238	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 722 as residues: Ser-78 to Trp-84, Pro-87 to Leu-94.
828573	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 723 as residues: Leu-9 to Thr-18, Leu-32 to Lys-37, Ser-45 to Leu-51, Val-80 to Glu-97, Pro-101 to Asp-108, Ala-115 to Glu-124, Ser-133 to Tyr-144, Glu-158 to Ser-165.
828848	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 726 as residues: Leu-8 to Ser-15, Arg-50 to Val-55, Gln-82 to Asp-88, Leu-96 to Ile-103, Thr-136 to Trp-141.
828929	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 727 as residues: His-2 to Leu-11, Glu-27 to Met-34, Ala-57 to Ser-72, Asn-119 to Phe-126.

829192	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 730 as residues: Ala-16 to Trp-28, Pro-36 to Gln-42, Glu-45 to Trp-50, Arg-137 to Ser-142, Ser-148 to Leu-153, Ile-178 to Gly-183, Asp-235 to Tyr-243.
829310	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 731 as residues: Cys-4 to Cys-14, Gly-86 to Ser-97.
829319	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 732 as residues: Asp-49 to Glu-54.
829459	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 733 as residues: His-1 to Thr-9.
829527	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 734 as residues: Gly-1 to Arg-8.
829736	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 735 as residues: Ala-1 to Lys-11, Arg-21 to Ser-26, Ser-45 to Ser-55, Tyr-115 to Asp-120, Asp-131 to Ile-145, Gln-147 to Asp-152, Ser-224 to Ser-231, Lys-252 to Glu-263, Ser-323 to Ser-332, His-341 to Asn-347.
830552	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 736 as residues: Phe-65 to Trp-73, Arg-87 to Gly-92, Gly-107 to Lys-112, Pro-177 to Thr-186.
830566	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 737 as residues: Pro-8 to Lys-19.
830569	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 739 as residues: Ser-37 to Trp-42, Ser-56 to Asp-61, Thr-68 to Asn-74, Lys-107 to Pro-113, Trp-133 to Arg-138, Asp-211 to Val-216, Pro-255 to Glu-260, Ser-293 to Ser-298, Cys-312 to Lys-322, Ser-374 to Asn-380, Gly-389 to Ile-399, Ser-403 to Ser-409, Ser-451 to Ser-462.
830583	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 740 as residues: Ala-5 to Gly-21, Gln-28 to Arg-37, Arg-67 to Ala-76, Glu-93 to Ala-100, Glu-117 to Arg-124, Lys-131 to Gly-145, Arg-152 to Met-160, Asp-176 to Glu-182, Asp-194 to Glu-203, Asp-231 to Glu-243, Lys-250 to Arg-257.
830716	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 744 as residues: Ala-5 to Arg-12, His-36 to Tyr-42, His-60 to Cys-75, Arg-87 to Gly-104, His-122 to Ser-140, Ser-163 to Pro-168, Thr-176 to Pro-181, Arg-195 to Pro-201.
830792	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 745 as residues: Cys-36 to Trp-43, Asn-113 to Ser-123, Pro-148 to Val-154, Glu-167 to Ser-172.
830893	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 746 as residues: Pro-33 to Trp-38, Arg-40 to Glu-46, Val-53 to Glu-58, Leu-66 to Leu-81, Leu-93 to Gln-98, Ile-145 to Asp-152.
831043	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 748 as residues: Glu-5 to Tyr-12, Ser-27 to Tyr-35.
831173	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 751 as residues: Ser-9 to Ser-14, Leu-41 to Gly-53, Thr-64 to Asn-71, Glu-78 to Thr-84.
831255	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 752 as residues: Gln-10 to Gly-21, Pro-39 to Pro-45.
831327	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 753 as residues: Gln-29 to Ile-42, Pro-45 to Ser-53, Cys-72 to Ser-77, Glu-98 to Ser-104, Asp-112 to Ser-122, Lys-130 to Ser-136, Ser-152 to Cys-162.
831493	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 754 as residues: Cys-1 to Gly-6, Pro-8 to Gln-19, Ser-29 to Cys-36, Pro-43 to Glu-64, Glu-70 to Thr-85.
831500	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 755 as residues: Ser-13 to Ala-25, Ser-64 to Gly-78, Glu-81 to Gln-89.
831502	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 757 as

	residues: Pro-19 to Phe-26, Pro-29 to Glv-34, Pro-50 to Ser-55.
831508	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 758 as residues: Asp-7 to Ser-14, Scr-42 to Ser-57.
831509	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 759 as residues: Glv-7 to Leu-13.
831520	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 760 as residues: Ser-17 to Glv-25.
831547	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 761 as residues: Ser-4 to Arg-10, Thr-89 to Trp-98, Thr-118 to Cys-124.
831847	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 764 as residues: Leu-27 to Lys-43.
831893	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 765 as residues: Lys-1 to Ser-18, Ile-20 to Val-27, Asp-44 to Thr-60.
831923	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 768 as residues: Pro-25 to Ser-33, Gln-113 to Ser-122, Trp-147 to Tyr-158, Scr-187 to Ala-198, His-201 to Glv-209, Pro-223 to Glv-228, Glu-233 to Glv-238.
831959	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 769 as residues: Tyr-46 to Glv-51.
832008	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 770 as residues: Ala-29 to Pro-48, Phe-79 to Thr-87, Glu-94 to Cys-101, Glu-111 to Asp-116.
832110	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 772 as residues: Val-2 to Leu-13, Ile-17 to Asn-22, Pro-49 to Ser-54, Ser-58 to Asp-74, Phe-107 to Ser-113, Gln-149 to Ser-159, Pro-166 to Lys-183, Scr-223 to Lys-229, Arg-251 to Glu-267, Ala-269 to Arg-275.
832146	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 773 as residues: Lys-26 to Ala-37, Pro-46 to Asn-52, Glu-137 to Pro-147, Scr-171 to Ser-185.
832189	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 774 as residues: Arg-20 to Asp-30, Pro-48 to Glv-53, Pro-67 to Glv-74.
832393	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 778 as residues: Glv-22 to Cys-29, Leu-52 to Phe-57, Phe-67 to Thr-73.
832448	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 781 as residues: Gly-2 to Arg-9, Leu-20 to Arg-28, Asp-33 to Arg-43, Lys-127 to Glu-132, His-146 to Pro-183.
832532	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 782 as residues: Val-4 to Ser-9, Lys-74 to Leu-79, Pro-95 to Lys-100, Asn-112 to Ile-117, Glu-129 to Ala-140, Asp-152 to Leu-158.
832621	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 783 as residues: Asp-17 to Glu-24, Glu-37 to Asn-44, Ile-53 to Gln-63, Glu-74 to Asp-82, Gln-91 to Lys-97, Leu-99 to Ile-104, Thr-114 to Ser-120.
832622	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 784 as residues: Leu-17 to Lys-36.
835327	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 785 as residues: Thr-40 to Glv-47.
835695	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 786 as residues: Gly-1 to Ile-11, Thr-23 to Ser-29.
835857	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 787 as residues: Leu-42 to Ser-54, Asp-82 to Ala-91, Lys-103 to Leu-111, Lys-117 to Asn-123, Glu-160 to Gln-165, Glu-183 to Val-192, Leu-225 to Lys-231, Lys-247 to Thr-255, Lys-279 to Asn-293, Leu-295 to Asn-303, Val-305 to Asn-317, Ile-360 to Cys-370, Leu-373 to Ala-385, Gln-413 to Ala-435, Pro-465 to Thr-489, Pro-491 to Gly-502, Pro-526 to Glu-534, Gln-550 to Val-559.

836183	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 788 as residues: Arg-57 to Thr-62.
836190	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 789 as residues: Val-34 to Ser-40.
836196	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 790 as residues: Arg-51 to Leu-57, Leu-61 to Ser-70, Ser-77 to Ser-84.
836253	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 791 as residues: Ser-1 to Thr-11.
836372	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 792 as residues: Gly-13 to Ser-30, Thr-38 to Trp-44, Ser-60 to Tyr-66, Asp-92 to Gln-99.
837445	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 794 as residues: Asn-1 to Gln-9, Lys-22 to Met-28, Gln-66 to Ser-73, Gln-76 to Gly-87, Ser-92 to Asp-99.
837620	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 795 as residues: Gln-11 to Gly-18, Ser-39 to Gln-44.
837995	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 797 as residues: Ser-44 to Ser-53, Thr-66 to Ser-71.
838237	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 799 as residues: Glu-62 to Asp-67, Gly-79 to Gly-85.
838700	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 800 as residues: Ser-88 to Lys-109, Lys-132 to Ile-137, Thr-158 to Asn-165, Asp-175 to Arg-191, Leu-199 to Gln-206, Leu-217 to Asp-222, Ser-229 to Ile-235, Gln-266 to Asn-271, Thr-293 to Gly-301, Tyr-321 to Asn-327, Phe-340 to Gln-348, Glu-415 to Asp-422, Gly-432 to Ser-439, Pro-443 to Arg-455, Asn-463 to Ser-470, Ser-478 to Cys-497, Ala-505 to Glu-552, Lys-558 to Lys-581.
839096	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 802 as residues: Arg-1 to Ser-17.
839588	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 804 as residues: Arg-41 to Glu-48.
839589	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 805 as residues: Arg-6 to His-13, Pro-69 to Glu-76.
839733	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 806 as residues: His-25 to His-31, Ser-61 to Gly-67, Pro-73 to Ala-80, Glu-123 to Ser-128, Glu-141 to Arg-149, Leu-162 to Gly-176, Ser-197 to Gly-204, Arg-222 to Asn-232, Gln-234 to Trp-242, Thr-250 to Val-257, Val-261 to Ala-271, Asp-301 to Thr-312, Pro-346 to Leu-352, Pro-355 to Cys-371, Ala-382 to Gly-394, Leu-435 to Asp-441, Pro-455 to Leu-460.
839874	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 807 as residues: Arg-98 to Thr-104, Gln-117 to Lys-122, Tyr-250 to Leu-262, Glu-296 to Lys-301.
840017	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 808 as residues: Ile-1 to Asp-6, Ser-42 to Asp-54, Ser-157 to Asn-166, Gly-188 to Ile-193, Glu-203 to Asp-208, Thr-236 to Lys-249, His-272 to Gln-278, Asn-364 to Glu-373, Ser-383 to Arg-388, Pro-391 to Ile-399, Gln-404 to Gly-412, Lys-420 to His-431.
840124	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 809 as residues: Gln-1 to Gly-8, Pro-17 to Trp-22.
840617	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 811 as residues: Thr-1 to Arg-6, Leu-22 to Glu-30, Lys-47 to Phe-61, Pro-131 to Asp-136, Arg-156 to Thr-161, Gln-181 to Trp-189, Glu-225 to Asp-234, Pro-251 to Thr-258, Ala-273 to Ser-278, Thr-285 to Arg-320, Pro-372 to Tyr-378, Val-380 to Ser-386, Asp-453 to Asn-460.
840792	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 813 as residues: Ala-1 to Gly-7, Ile-17 to Gly-38, Asn-50 to Lys-58, Gln-61 to Gln-68, Ser-

	80 to Val-86, Asp-182 to Ser-190.
841325	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 816 as residues: Arg-28 to Glu-90, Phe-94 to Ser-104, Leu-123 to Lys-129, Lys-147 to Gly-152.
841713	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 817 as residues: Ser-36 to Arg-46, Thr-52 to Asp-64, Ser-69 to Gly-89, Ser-96 to Asp-102, Ile-106 to Phe-120, Val-136 to Thr-142, Gly-146 to Asp-169, Lys-176 to Phe-182, Asp-200 to Ser-206.
842454	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 820 as residues: Glv-41 to Glv-53, Glv-65 to Arg-77.
842768	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 821 as residues: Thr-7 to Thr-13, Arg-49 to Gln-55.
842999	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 822 as residues: Leu-25 to Glu-32.
843830	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 823 as residues: Asp-24 to Asp-31, Gly-37 to Thr-47, Gly-55 to Ala-60, Gly-91 to Asn-107, Glu-113 to Glu-120.
844723	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 824 as residues: Glv-1 to Glv-7, Glv-14 to Glv-20.
844868	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 825 as residues: Pro-19 to Glv-40, Lys-54 to Ala-60, Lys-69 to Asn-74, Asn-80 to Pro-94.
845373	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 827 as residues: Tyr-3 to Gly-11, Arg-68 to Trp-76, Pro-82 to Ile-91, Asn-138 to Ala-144, Arg-169 to Lys-175, Ser-180 to Glu-192, Ile-421 to Ser-427.
845412	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 828 as residues: Cys-24 to Gly-35, Ala-42 to Glu-47, Gln-181 to Asp-188, Pro-277 to His-292.
HISED43R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 829 as residues: Lys-1 to Trp-6, Gln-9 to Gln-16, Glv-66 to Val-71, Lys-74 to Trp-82.
HOSEQ76R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 830 as residues: Ser-36 to Gly-48.
HISDS43R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 831 as residues: Ser-28 to Arg-36.
HPJDY28R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 832 as residues: Cys-9 to His-14.
HISDW59R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 837 as residues: Ile-4 to Val-9.
HTPGD92R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 839 as residues: Ser-9 to Pro-14.
HHFLB69R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 840 as residues: Pro-1 to Gly-6, Pro-20 to Arg-25, Ala-45 to Ser-50.
HPDEH50R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 841 as residues: Ser-24 to Ser-29.
HMTMA16R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 842 as residues: Cys-4 to Gly-11, Ile-59 to Gln-64, Asn-85 to Lys-90, Glu-94 to Lys-99.
HTPGL88R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 844 as residues: Ala-30 to Gly-42, Leu-44 to Lys-50, Gln-60 to Asp-68, Gln-78 to Ser-84.
HMCIA86R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 845 as residues: Glv-39 to Ser-45, Arg-52 to Arg-58.
HDTFE89R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 847 as residues: Glu-25 to Gln-32.
HTLHH34R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 850 as residues: Phe-11 to Ser-22, Ser-79 to Lys-86, His-97 to Asp-102.

HCCMA63R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 855 as residues: Glv-1 to Glv-13.
HE8EZ73R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 856 as residues: Ala-1 to Leu-7, Ile-14 to Gln-22, Glu-39 to Asp-44, Leu-76 to Val-84, Asn-89 to Leu-95, Pro-98 to Glu-103.
HALSD82R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 858 as residues: Asn-1 to Asp-6, Thr-19 to Cys-31, Glu-33 to Trp-39, Gly-56 to Asp-69, Met-84 to His-106, Lys-112 to His-118.
H2LAS44R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 859 as residues: His-10 to Gln-18, Ser-79 to Glv-89.
HTXPA42R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 860 as residues: Arg-1 to Lys-6, Asn-31 to Lys-39.
HAHEJ39R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 862 as residues: Asp-8 to Glv-14, Glv-19 to Ser-29, Arg-67 to Glv-72.
HOEMQ04R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 863 as residues: Lys-12 to Arg-21, Tyr-57 to Pro-71.
HOENU56R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 865 as residues: Leu-9 to Leu-15.
HAGGB37R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 866 as residues: Asn-32 to His-38.
HAHDO57R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 868 as residues: Glv-1 to Glv-7, Glv-17 to Ser-28.
HTPCT95R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 871 as residues: Glu-33 to Trp-40, Tyr-48 to His-56.
HCCMD33R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 873 as residues: Glu-9 to Glv-14, Cys-33 to Lys-44.
HCE4L96R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 875 as residues: Gln-1 to Arg-8, Arg-13 to Ser-30, His-38 to Tyr-44.
HTPGL86R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 876 as residues: Gln-47 to Cys-53, Asn-66 to Cys-71.
HWDK95R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 878 as residues: His-17 to Gln-26, Met-28 to His-39, Pro-48 to Glv-58.
HE9DG72R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 879 as residues: Val-29 to Lys-34, Thr-50 to Gly-56.
HDPOY89R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 880 as residues: Gln-1 to Met-11, Pro-26 to Ser-37, Pro-55 to His-60, Lys-83 to Thr-99.
HAHEJ13R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 881 as residues: Glu-12 to Ser-17.
HCFCM83R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 883 as residues: Glu-19 to Ala-26.
HBMBJ92R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 891 as residues: Leu-22 to Glv-27, Glu-33 to Val-38.
HCGBC37R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 892 as residues: Phe-26 to Val-31, Pro-35 to Arg-42.
HCROI22R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 893 as residues: Pro-5 to Ser-14, Ser-25 to Leu-30.
HDTLK21R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 894 as residues: Pro-11 to Asn-17.
HEGAD29R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 898 as residues: Glu-1 to His-6, Glv-19 to Trp-31.
HFKHC10R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 899 as residues: Val-12 to Asn-18, Lys-30 to Glu-38.
HNHGQ70R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 909 as

	residues: Pro-6 to Ala-16. Ala-61 to Met-68. Pro-72 to Ala-77. Ser-88 to His-93. Thr-113 to Ser-118.
HOSMV19R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 910 as residues: Pro-12 to Leu-18.
HULEB88R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 913 as residues: Glu-11 to Leu-17. Leu-36 to Thr-41.
HWLWG5S R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 917 as residues: Glu-1 to Cys-6.
HAIDL46R	Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 918 as residues: His-1 to Asp-55. Asp-57 to His-74.

The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of the polypeptide sequence shown in SEQ ID NO:Y, or an epitope of the polypeptide sequence encoded by the cDNA in the related cDNA clone contained in a deposited library or encoded by a polynucleotide that hybridizes to the complement of an epitope encoding sequence of SEQ ID NO:X, or an epitope encoding sequence contained in the deposited cDNA clone under stringent hybridization conditions, or alternatively, under lower stringency hybridization conditions, as defined supra. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to this complementary strand under stringent hybridization conditions or alternatively, under lower stringency hybridization conditions, as defined supra.

The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies described infra. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross- reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).

Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol. 66:2347-2354 (1985)). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, in vivo immunization, in vitro immunization, and phage display methods. See, e.g., Sutcliffe et al., *supra*; Wilson et al., *supra*, and Bittle et al., *J. Gen. Virol.*, 66:2347-2354 (1985). If in vivo immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 µg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention, and immunogenic and/or antigenic epitope fragments thereof can be fused to other polypeptide sequences. For example, the polypeptides of the present invention may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof) resulting in chimeric polypeptides. Such fusion proteins may facilitate purification and may increase half-life in vivo. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light

chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., Nature, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG Fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion disulfide bonds have also been found to be more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., J. Biochem., 270:3958-3964 (1995).

10 Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, may be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, 15 D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).)

Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope 25

derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

5 Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin ("HA") tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., Proc. Natl. Acad. Sci. USA 10 88:8972- 897 (1991)). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni²⁺ nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing 15 buffers.

Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to 20 modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458. and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. 25 Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308- 13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of polynucleotides corresponding to SEQ ID NO:X and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA 30 segments by homologous or site-specific recombination to generate variation in the

polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

As discussed herein, any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, polypeptides of the present invention which are shown to be secreted can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

In certain preferred embodiments, proteins of the invention comprise fusion proteins wherein the polypeptides are N and/or C- terminal deletion mutants. In preferred embodiments, the application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to the nucleic acid sequences encoding polypeptides having the amino acid sequence of the specific N- and C-terminal deletions mutants. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell

or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

5

Vectors, Host Cells, and Protein Production

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In
10 the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides of the invention may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced
15 in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac
20 promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a
25 translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin
30 resistance genes for culturing in E. coli and other bacteria. Representative examples

of appropriate hosts include, but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells (e.g., *Saccharomyces cerevisiae* or *Pichia pastoris* (ATCC Accession No. 201178)); insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors. Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlsbad, CA). Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., *Basic Methods In Molecular Biology* (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most

preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether
5 directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition,
10 polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed
15 in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

In one embodiment, the yeast *Pichia pastoris* is used to express polypeptides of the invention in a eukaryotic system. *Pichia pastoris* is a methylotrophic yeast
20 which can metabolize methanol as its sole carbon source. A main step in the methanol metabolism pathway is the oxidation of methanol to formaldehyde using O_2 . This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, *Pichia pastoris* must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O_2 .
25 Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (*AOX1*) is highly active. In the presence of methanol, alcohol oxidase produced from the *AOX1* gene comprises up to approximately 30% of the total soluble protein in *Pichia pastoris*. See, Ellis, S.B., et al., *Mol. Cell. Biol.* 5:1111-21 (1985); Koutz, P.J. et al., *Yeast*

5:167-77 (1989); Tschopp, J.F., *et al.*, *Nucl. Acids Res.* 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the *AOX1* regulatory sequence is expressed at exceptionally high levels in *Pichia* yeast grown in the presence of methanol.

10 In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "*Pichia* Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector allows expression and secretion of a polypeptide of the invention by virtue of the strong *AOX1* promoter linked to the *Pichia pastoris* alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

15 Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as long as the proposed expression construct provides appropriately located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

20 In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

25 In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and

which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

10 In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983. Proteins: Structures and Molecular Principles, W.H. Freeman & Co., N.Y., and Hunkapiller et al., *Nature*, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide can be synthesized by use of a peptide synthesizer. Furthermore, if
15 desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid, α -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid,
20 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoro-amino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L
25 (levorotary).

Non-naturally occurring variants may be produced using art-known mutagenesis techniques, which include, but are not limited to oligonucleotide mediated mutagenesis, alanine scanning, PCR mutagenesis, site directed mutagenesis (see, e.g., Carter et al., *Nucl. Acids Res.* 13:4331 (1986); and Zoller et al., *Nucl. Acids Res.* 10:6487 (1982)), cassette mutagenesis (see, e.g., Wells et al., *Gene* 34:315

(1985)), restriction selection mutagenesis (*see. e.g., Wells et al., Philos. Trans. R. Soc. London SerA 317:415 (1986)*).

The invention additionally, encompasses polypeptides of the present invention which are differentially modified during or after translation. e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between

about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release
5 desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example, the polyethylene glycol may have an average molecular weight of about 200; 500; 1000; 1500; 2000; 2500; 3000; 3500; 4000; 4500; 5000; 5500; 6000; 6500; 7000; 7500; 8000; 8500; 9000; 9500; 10,000;
10 10,500; 11,000; 11,500; 12,000; 12,500; 13,000; 13,500; 14,000; 14,500; 15,000; 15,500; 16,000; 16,500; 17,000; 17,500; 18,000; 18,500; 19,000; 19,500; 20,000; 25,000; 30,000; 35,000; 40,000; 50,000; 55,000; 60,000; 65,000; 70,000; 75,000; 80,000; 85,000; 90,000; 95,000; or 100,000 kDa.

As noted above, the polyethylene glycol may have a branched structure.
15 Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo *et al.*, *Appl. Biochem. Biotechnol.* 56:59-72 (1996); Vorobjev *et al.*, *Nucleosides Nucleotides* 18:2745-2750 (1999); and Caliceti *et al.*, *Bioconjug. Chem.* 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

20 The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, e.g., EP 0 401 384, herein incorporated by reference (coupling PEG to G-CSF), see also Malik *et al.*, *Exp. Hematol.* 20:1028-1035 (1992) (reporting
25 pegylation of GM-CSF using tresyl chloride). For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as, a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues;
30 those having a free carboxyl group may include aspartic acid residues glutamic acid

residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

5 As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to a proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine,
10 histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may
15 select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this
20 moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for
25 derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be
30 attached to the protein either directly or by an intervening linker. Linkerless systems

for attaching polyethylene glycol to proteins are described in Delgado *et al.*, *Crit. Rev. Thera. Drug Carrier Sys.* 9:249-304 (1992); Francis *et al.*, *Intern. J. of Hematol.* 68:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated
5 herein by reference.

One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride ($\text{ClSO}_2\text{CH}_2\text{CF}_3$). Upon reaction of protein with tresylated MPEG,
10 polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoroethane sulphonyl group.

Polyethylene glycol can also be attached to proteins using a number of
15 different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-
20 succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number additional polyethylene glycol derivatives and reaction chemistries for attaching polyethylene glycol to proteins are described in WO 98/32466, the entire disclosure of which is incorporated herein by reference.
25 Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

The number of polyethylene glycol moieties attached to each protein of the invention (*i.e.*, the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12,
30 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of

substitution within ranges such as 1-3, 2-4, 3-5, 4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado *et al.*, *Crit. Rev. Thera. Drug Carrier Sys.* 9:249-304 (1992).

The pancreatic cancer antigen polypeptides of the invention may be in monomers or multimers (i.e., dimers, trimers, tetramers and higher multimers). Accordingly, the present invention relates to monomers and multimers of the polypeptides of the invention, their preparation, and compositions (preferably, Therapeutics) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers, or at least tetramers.

Multimers encompassed by the invention may be homomers or heteromers. As used herein, the term homomer, refers to a multimer containing only polypeptides corresponding to the amino acid sequence of SEQ ID NO:Y or an amino acid sequence encoded by SEQ ID NO:X, and/or an amino acid sequence encoded by the cDNA in a related cDNA clone contained in a deposited library (including fragments, variants, splice variants, and fusion proteins, corresponding to any one of these as described herein). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid sequence. In another specific embodiment, a homomer of the invention is a multimer containing polypeptides having different amino acid sequences. In specific embodiments, the multimer of the invention is a homodimer (e.g., containing polypeptides having identical or different amino acid sequences) or a homotrimer (e.g., containing polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at least a homotrimer, or at least a homotetramer.

As used herein, the term heteromer refers to a multimer containing one or more heterologous polypeptides (i.e., polypeptides of different proteins) in addition to

the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

5 Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked, by for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers
10 of the invention, such as, for example, heterotrimers or heterotetramers, are formed when polypeptides of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides
15 of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence (e.g., that recited in SEQ ID NO:Y, or contained in a polypeptide encoded by SEQ ID NO:X, and/or by the cDNA in the related cDNA clone contained in a deposited library). In one instance, the covalent associations are cross-linking between cysteine residues located within the
20 polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a fusion protein. In one example, covalent associations are between the
25 heterologous sequence contained in a fusion protein of the invention (see, e.g., US Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from
30 another protein that is capable of forming covalently associated multimers, such as for

example, osteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., Science 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.

Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (FEBS Letters 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.

In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention

containing Flag® polypeptide sequence. In a further embodiment, associations of the invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

5 The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).
10 Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely
15 modified by the addition of cysteine or biotin to the C-terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the
20 polypeptide components desired to be contained in the multimer of the invention (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

 Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained
25 in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the
30 invention to a sequence encoding a linker polypeptide and then further to a synthetic

polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described
5 herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hydrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

10

Antibodies

Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of SEQ ID NO:Y, and/or an epitope, of the present invention (as
15 determined by immunoassays well known in the art for assaying specific antibody-antigen binding). Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id
20 antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass
25 of immunoglobulin molecule.

Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')₂, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and
30 fragments comprising either a VL or VH domain. Antigen-binding antibody

fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, ship rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, or by size in contiguous amino acid residues. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog,

or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or K_d less than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein. In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85 %, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50%.

Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described supra). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res.

58(16):3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998); Prat et al., J. Cell. Sci. 111(Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautard et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

Antibodies of the present invention may be used, for example, but not limited to, to purify, detect, and target the polypeptides of the present invention, including both in vitro and in vivo diagnostic and therapeutic methods. For example, the antibodies have use in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988) (incorporated by reference herein in its entirety).

As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalently and non-covalently conjugations) to polypeptides or other compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387.

The antibodies of the invention include derivatives that are modified, i.e., by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups,

proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

The antibodies of the present invention may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of-interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples. In a non-limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')₂ fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). F(ab')₂ fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain.

For example, the antibodies of the present invention can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire

or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., J. Immunol. Methods 182:41-50 (1995); Ames et al., J. Immunol. Methods 184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')₂ fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999

(1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol. Methods 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entirety.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody

libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

5 Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the
10 human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous
15 deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention.
20 Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG,
25 IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, Int. Rev. Immunol. 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European
30 Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825;

5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., Bio/technology 12:899-903 (1988)).

Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotypic antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, FASEB J. 7(5):437-444; (1989) and Nissinoff, J. Immunol. 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand. For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligands/receptors, and thereby block its biological activity.

Polynucleotides Encoding Antibodies

The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or alternatively, under lower stringency hybridization conditions, e.g., as defined supra, to polynucleotides that encode an antibody, preferably, that specifically binds to a

polypeptide of the invention. preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y.

The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody
5 may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., *BioTechniques* 17:242 (1994)), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of
10 the ligated oligonucleotides by PCR.

Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized
15 or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe
20 specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence and corresponding amino acid sequence of the
25 antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, *Molecular Cloning, A Laboratory Manual*, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY
30 and Ausubel et al., eds., 1998, *Current Protocols in Molecular Biology*, John Wiley &

Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well known in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a non-human antibody, as described supra. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed supra, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described supra, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived

from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird. Science 242:423- 42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in E. coli may also be used (Skerra et al., Science 242:1038- 1041 (1988)).

Methods of Producing Antibodies

The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof. (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The invention, thus, provides replicable vectors comprising a

nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT
5 Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an
10 antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell
15 for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with
20 the appropriate nucleotide coding sequences, express an antibody molecule of the invention in situ. These include but are not limited to microorganisms such as bacteria (e.g., *E. coli*, *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., *Saccharomyces*, *Pichia*) transformed with recombinant yeast
25 expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid)
30 containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO,

BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter: the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as *Escherichia coli*,
5 and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for
10 antibodies (Foecking et al., *Gene* 45:101 (1986); Cockett et al., *Bio/Technology* 8:2 (1990)).

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the
15 generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the *E. coli* expression vector pUR278 (Ruther et al., *EMBO J.* 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding
20 region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, *Nucleic Acids Res.* 13:3101-3109 (1985); Van Heeke & Schuster, *J. Biol. Chem.* 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by
25 adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, *Autographa californica* nuclear polyhedrosis virus
30 (AcNPV) is used as a vector to express foreign genes. The virus grows in

Spodoptera frugiperda cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

5 In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by in vitro or in vivo
10 recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the
15 ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate
20 transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g.,
25 cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which
30 possess the cellular machinery for proper processing of the primary transcript,

glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, HeLa, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed in tk-, hgp^rt- or ap^rt- cells, respectively.

Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 Clinical Pharmacy 12:488-505; Wu and Wu, Biotherapy 3:87-95 (1991);

Tolstoshev, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596 (1993); Mulligan, *Science* 260:926-932 (1993); and Morgan and Anderson, *Ann. Rev. Biochem.* 62:191-217 (1993); May, 1993, *TIB TECH* 11(5):155-215; and hygromycin, which confers resistance to hygromycin (Santerre et al., *Gene* 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, NY (1993); Kriegler, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), *Current Protocols in Human Genetics*, John Wiley & Sons, NY (1994); Colberre-Garapin et al., *J. Mol. Biol.* 150:1 (1981), which are incorporated by reference herein in their entireties.

The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, *The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning*, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., *Mol. Cell. Biol.* 3:257 (1983)).

The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, *Nature* 322:52 (1986); Kohler, *Proc. Natl. Acad. Sci. USA* 77:2197 (1980)). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

Once an antibody molecule of the invention has been produced by an animal, chemically synthesized, or recombinantly expressed, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. In addition, the antibodies of the present invention or fragments thereof can be fused to heterologous polypeptide sequences described herein or otherwise known in the art, to facilitate purification.

The present invention encompasses antibodies recombinantly fused or chemically conjugated (including both covalently and non-covalently conjugations) to a polypeptide (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. The antibodies may be specific for antigens other than polypeptides (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention. For example, antibodies may be used to target the polypeptides of the present invention to particular cell types, either in vitro or in vivo, by fusing or conjugating the polypeptides of the present invention to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to the polypeptides of the present invention may also be used in in vitro immunoassays and purification methods using methods known in the art. See e.g., Harbor et al., supra, and PCT publication WO 93/21232; EP 439,095; Naramura et al., Immunol. Lett. 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., PNAS 89:1428-1432 (1992); Fell et al., J. Immunol. 146:2446-2452(1991), which are incorporated by reference in their entireties.

The present invention further includes compositions comprising the polypeptides of the present invention fused or conjugated to antibody domains other than the variable regions. For example, the polypeptides of the present invention may be fused or conjugated to an antibody Fc region, or portion thereof. The antibody

portion fused to a polypeptide of the present invention may comprise the constant region, hinge region, CH1 domain, CH2 domain, and CH3 domain or any combination of whole domains or portions thereof. The polypeptides may also be fused or conjugated to the above antibody portions to form multimers. For example, Fc portions fused to the polypeptides of the present invention can form dimers through disulfide bonding between the Fc portions. Higher multimeric forms can be made by fusing the polypeptides to portions of IgA and IgM. Methods for fusing or conjugating the polypeptides of the present invention to antibody portions are known in the art. See, e.g., U.S. Patent Nos. 5,336,603; 5,622,929; 5,359,046; 5,349,053; 5,447,851; 5,112,946; EP 307,434; EP 367,166; PCT publications WO 96/04388; WO 91/06570; Ashkenazi et al., Proc. Natl. Acad. Sci. USA 88:10535-10539 (1991); Zheng et al., J. Immunol. 154:5590-5600 (1995); and Vil et al., Proc. Natl. Acad. Sci. USA 89:11337-11341(1992) (said references incorporated by reference in their entireties).

As discussed, supra, the polypeptides corresponding to a polypeptide, polypeptide fragment, or a variant of SEQ ID NO:Y may be fused or conjugated to the above antibody portions to increase the in vivo half life of the polypeptides or for use in immunoassays using methods known in the art. Further, the polypeptides corresponding to SEQ ID NO:Y may be fused or conjugated to the above antibody portions to facilitate purification. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP 394,827; Traunecker et al., Nature 331:84-86 (1988). The polypeptides of the present invention fused or conjugated to an antibody having disulfide- linked dimeric structures (due to the IgG) may also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995)). In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP A 232,262). Alternatively, deleting the Fc part after the fusion protein has been

expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, Bennett et al., J. Molecular Recognition 8:52-58 (1995); Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).

Moreover, the antibodies or fragments thereof of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the "HA" tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)) and the "flag" tag.

The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Patent No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention. Examples of suitable enzymes include horseradish

peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine
5 fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include ¹²⁵I, ¹³¹I, ¹¹¹In or ⁹⁹Tc.

Further, an antibody or fragment thereof may be conjugated to a therapeutic
10 moiety such as a cytotoxin, e.g., a cytostatic or cytotoxic agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, ²¹³Bi. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin,
15 dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine,
20 thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic
25 agents (e.g., vincristine and vinblastine).

The conjugates of the invention can be used for modifying a given biological response, the therapeutic agent or drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include,
30 for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria

toxin; a protein such as tumor necrosis factor, α -interferon, β -interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, e.g., TNF- α , TNF- β , AIM I (See, International Publication No. WO 97/33899), AIM II (See, International Publication No. WO 97/34911), Fas Ligand (Takahashi *et al.*, *Int. Immunol.*, 6:1567-1574 (1994)), VEGF (See, International Publication No. WO 99/23105), a thrombotic agent or an anti-angiogenic agent, e.g., angiostatin or endostatin; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Techniques for conjugating such therapeutic moiety to antibodies are well known, see, e.g., Arnon *et al.*, "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in *Monoclonal Antibodies And Cancer Therapy*, Reisfeld *et al.* (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom *et al.*, "Antibodies For Drug Delivery", in *Controlled Drug Delivery* (2nd Ed.), Robinson *et al.* (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera *et al.* (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in *Monoclonal Antibodies For Cancer Detection And Therapy*, Baldwin *et al.* (eds.), pp. 303-16 (Academic Press 1985), and Thorpe *et al.*, "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", *Immunol. Rev.* 62:119-58 (1982).

Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

An antibody, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

5 ***Immunophenotyping***

The antibodies of the invention may be utilized for immunophenotyping of cell lines and biological samples. The translation product of the gene of the present invention may be useful as a cell specific marker, or more specifically as a cellular marker that is differentially expressed at various stages of differentiation and/or maturation of particular cell types. Monoclonal antibodies directed against a specific epitope, or combination of epitopes, will allow for the screening of cellular populations expressing the marker. Various techniques can be utilized using monoclonal antibodies to screen for cellular populations expressing the marker(s), and include magnetic separation using antibody-coated magnetic beads, "panning" with antibody attached to a solid matrix (i.e., plate), and flow cytometry (See, e.g., U.S. Patent 5,985,660; and Morrison *et al.*, *Cell*, 96:737-49 (1999)).

These techniques allow for the screening of particular populations of cells, such as might be found with hematological malignancies (i.e. minimal residual disease (MRD) in acute leukemic patients) and "non-self" cells in transplantations to prevent Graft-versus-Host Disease (GVHD). Alternatively, these techniques allow for the screening of hematopoietic stem and progenitor cells capable of undergoing proliferation and/or differentiation, as might be found in human umbilical cord blood.

Assays For Antibody Binding

The antibodies of the invention may be assayed for immunospecific binding by any method known in the art. The immunoassays which can be used include but are not limited to competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays,

complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1. John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

Immunoprecipitation protocols generally comprise lysing a population of cells in a lysis buffer such as RIPA buffer (1% NP-40 or Triton X- 100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 0.01 M sodium phosphate at pH 7.2, 1% Trasyolol) supplemented with protein phosphatase and/or protease inhibitors (e.g., EDTA, PMSF, aprotinin, sodium vanadate), adding the antibody of interest to the cell lysate, incubating for a period of time (e.g., 1-4 hours) at 4° C, adding protein A and/or protein G sepharose beads to the cell lysate, incubating for about an hour or more at 4° C, washing the beads in lysis buffer and resuspending the beads in SDS/sample buffer. The ability of the antibody of interest to immunoprecipitate a particular antigen can be assessed by, e.g., western blot analysis. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the binding of the antibody to an antigen and decrease the background (e.g., pre-clearing the cell lysate with sepharose beads). For further discussion regarding immunoprecipitation protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.16.1.

Western blot analysis generally comprises preparing protein samples, electrophoresis of the protein samples in a polyacrylamide gel (e.g., 8%- 20% SDS-PAGE depending on the molecular weight of the antigen), transferring the protein sample from the polyacrylamide gel to a membrane such as nitrocellulose, PVDF or nylon, blocking the membrane in blocking solution (e.g., PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (e.g., PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, e.g., an anti-human

antibody) conjugated to an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) or radioactive molecule (e.g., ^{32}P or ^{125}I) diluted in blocking buffer. washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.8.1.

ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the art. For further discussion regarding ELISAs see, e.g., Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 11.2.1.

The binding affinity of an antibody to an antigen and the off-rate of an antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (e.g., ^3H or ^{125}I) with the antibody of interest in the presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of interest for a particular antigen and the binding off-rates can be determined from the data by

scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays. In this case, the antigen is incubated with antibody of interest conjugated to a labeled compound (e.g., ^3H or ^{125}I) in the presence of increasing amounts of an unlabeled second antibody.

5

Therapeutic Uses

The present invention is further directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the disclosed
10 diseases, disorders, or conditions. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to treat,
15 inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions described herein. The treatment and/or prevention of diseases, disorders, or conditions associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is
20 not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the
25 present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes
30 without undue experimentation.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, e.g., IL-2, IL-3 and IL-7), for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

The antibodies of the invention may be administered alone or in combination with other types of treatments (e.g., radiation therapy, chemotherapy, hormonal therapy, immunotherapy and anti-tumor agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides of the invention, including fragments thereof. Preferred binding affinities include those with a dissociation constant or K_d less than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, and 10^{-15} M.

25 *Gene Therapy*

In a specific embodiment, nucleic acids comprising sequences encoding antibodies or functional derivatives thereof, are administered to treat, inhibit or prevent a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic

acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

5 For general reviews of the methods of gene therapy, see Goldspiel et al., Clinical Pharmacy 12:488-505 (1993); Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, TIBTECH 11(5):155-215 (1993). Methods commonly known in the art
10 of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons. NY (1993); and Kriegler, Gene Transfer and Expression. A Laboratory Manual. Stockton Press, NY (1990).

In a preferred aspect, the compound comprises nucleic acid sequences
15 encoding an antibody, said nucleic acid sequences being part of expression vectors that express the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment,
20 nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody encoding nucleic acids (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989). In
25 specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.

Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vectors, or
30 indirect, in which case, cells are first transformed with the nucleic acids in vitro, then

transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid sequences are directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)).

In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention are used. For example, a retroviral vector can be used (see Miller et al., Meth. Enzymol. 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which

facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., *Biotherapy* 6:291-302 (1994), which describes the use of a retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., *J. Clin. Invest.* 93:644-651 (1994); Kiem et al., *Blood* 83:1467-1473 (1994); Salmons and Gunzberg, *Human Gene Therapy* 4:129-141 (1993); and Grossman and Wilson, *Curr. Opin. in Genetics and Devel.* 3:110-114 (1993).

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, *Current Opinion in Genetics and Development* 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., *Human Gene Therapy* 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., *Science* 252:431-434 (1991); Rosenfeld et al., *Cell* 68:143-155 (1992); Mastrangeli et al., *J. Clin. Invest.* 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., *Gene Therapy* 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., *Proc. Soc. Exp. Biol. Med.* 204:289-300 (1993); U.S. Patent No. 5,436,146).

Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection

to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, Meth. Enzymol. 217:599-618 (1993); Cohen et al., Meth. Enzymol. 217:618-644 (1993); Cline, Pharmac. Ther. 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as Tlymphocytes, Blymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, Cell 71:973-985 (1992); Rheinwald, Meth. Cell Bio. 21A:229 (1980); and Pittelkow and Scott, Mayo Clinic Proc. 61:771 (1986)).

10 In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription. Demonstration of Therapeutic or Prophylactic Activity

15 The compounds or pharmaceutical compositions of the invention are preferably tested in vitro, and then in vivo for the desired therapeutic or prophylactic activity, prior to use in humans. For example, in vitro assays to demonstrate the therapeutic or prophylactic utility of a compound or pharmaceutical composition include, the effect of a compound on a cell line or a patient tissue sample. The effect of the compound or composition on the cell line and/or tissue sample can be determined utilizing techniques known to those of skill in the art including, but not limited to, rosette formation assays and cell lysis assays. In accordance with the invention, in vitro assays which can be used to determine whether administration of a specific compound is indicated, include in vitro cell culture assays in which a patient tissue sample is grown in culture, and exposed to or otherwise administered a compound, and the effect of such compound upon the tissue sample is observed.

Therapeutic/Prophylactic Administration and Composition

30 The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical

composition of the invention, preferably a polypeptide or antibody of the invention. In a preferred aspect, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce undesired side-effects). The subject is preferably an animal, including but not limited to animals such as cows, pigs, horses,
5 chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.

Formulations and methods of administration that can be employed when the compound comprises a nucleic acid or an immunoglobulin are described above; additional appropriate formulations and routes of administration can be selected from among those described herein below.

10 Various delivery systems are known and can be used to administer a compound of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the compound, receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of
15 introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds or compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together
20 with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such
25 as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion
30 during surgery, topical application, e.g., in conjunction with a wound dressing after

surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when administering a protein, including an antibody, of the invention, care must be taken to use materials to which the protein does not absorb.

In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, *Science* 249:1527-1533 (1990); Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353- 365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton, *CRC Crit. Ref. Biomed. Eng.* 14:201 (1987); Buchwald et al., *Surgery* 88:507 (1980); Saudek et al., *N. Engl. J. Med.* 321:574 (1989)). In another embodiment, polymeric materials can be used (see *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., *Macromol. Sci. Rev. Macromol. Chem.* 23:61 (1983); see also Levy et al., *Science* 228:190 (1985); During et al., *Ann. Neurol.* 25:351 (1989); Howard et al., *J. Neurosurg.* 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138 (1984)).

Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

In a specific embodiment where the compound of the invention is a nucleic acid encoding a protein, the nucleic acid can be administered in vivo to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by

use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox- like peptide which is known to enter the nucleus (see e.g.,
5 Joliot et al., Proc. Natl. Acad. Sci. USA 88:1864-1868 (1991)), etc. Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a
10 pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the
15 therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as
20 liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH
25 buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate,
30 sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable

pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation
5 should suit the mode of administration.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the
10 composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the
15 composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compounds of the invention can be formulated as neutral or salt forms.
20 Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

25 The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the
30 formulation will also depend on the route of administration, and the seriousness of

the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the antibodies by modifications such as, for example, lipidation.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

20

Diagnosis and Imaging

Labeled antibodies, and derivatives and analogs thereof, which specifically bind to a polypeptide of interest can be used for diagnostic purposes to detect, diagnose, or monitor diseases, disorders, and/or conditions associated with the aberrant expression and/or activity of a polypeptide of the invention. The invention provides for the detection of aberrant expression of a polypeptide of interest, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level,

whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of aberrant expression.

The invention provides a diagnostic assay for diagnosing a disorder, comprising (a) assaying the expression of the polypeptide of interest in cells or body
5 fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a particular disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied
10 tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

15 Antibodies of the invention can be used to assay protein levels in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell . Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked
20 immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (^{125}I , ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium (^{112}In), and technetium (^{99}Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

25 One aspect of the invention is the detection and diagnosis of a disease or disorder associated with aberrant expression of a polypeptide of interest in an animal, preferably a mammal and most preferably a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled molecule which
30 specifically binds to the polypeptide of interest; b) waiting for a time interval

following the administering for permitting the labeled molecule to preferentially concentrate at sites in the subject where the polypeptide is expressed (and for unbound labeled molecule to be cleared to background level); c) determining background level; and d) detecting the labeled molecule in the subject, such that
5 detection of labeled molecule above the background level indicates that the subject has a particular disease or disorder associated with aberrant expression of the polypeptide of interest. Background level can be determined by various methods including, comparing the amount of labeled molecule detected to a standard value previously determined for a particular system.

10 It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of ^{99m}Tc. The labeled antibody or antibody fragment will then preferentially
15 accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).

20 Depending on several variables, including the type of label used and the mode of administration, the time interval following the administration for permitting the labeled molecule to preferentially concentrate at sites in the subject and for unbound labeled molecule to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5
25 to 20 days or 5 to 10 days.

In an embodiment, monitoring of the disease or disorder is carried out by repeating the method for diagnosing the disease or disease. for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, etc.

Presence of the labeled molecule can be detected in the patient using methods known in the art for in vivo scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods of the invention include, but are not limited to, computed tomography (CT), whole body scan such as position emission tomography (PET), magnetic resonance imaging (MRI), and sonography.

In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston et al., U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patent using positron emission-tomography. In yet another embodiment, the molecule is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

Kits

The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises an antibody of the invention, preferably a purified antibody, in one or more containers. In a specific embodiment, the kits of the present invention contain a substantially isolated polypeptide comprising an epitope which is specifically immunoreactive with an antibody included in the kit. Preferably, the kits of the present invention further comprise a control antibody which does not react with the polypeptide of interest. In another specific embodiment, the kits of the present invention contain a means for detecting the binding of an antibody to a polypeptide of interest (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate).

In another specific embodiment of the present invention, the kit is a diagnostic kit for use in screening serum containing antibodies specific against proliferative and/or cancerous polynucleotides and polypeptides. Such a kit may include a control antibody that does not react with the polypeptide of interest. Such a kit may include a substantially isolated polypeptide antigen comprising an epitope which is specifically immunoreactive with at least one anti-polypeptide antigen antibody. Further, such a kit includes means for detecting the binding of said antibody to the antigen (e.g., the antibody may be conjugated to a fluorescent compound such as fluorescein or rhodamine which can be detected by flow cytometry). In specific embodiments, the kit may include a recombinantly produced or chemically synthesized polypeptide antigen. The polypeptide antigen of the kit may also be attached to a solid support.

In a more specific embodiment the detecting means of the above-described kit includes a solid support to which said polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the polypeptide antigen can be detected by binding of the said reporter-labeled antibody.

In an additional embodiment, the invention includes a diagnostic kit for use in screening serum containing antigens of the polypeptide of the invention. The diagnostic kit includes a substantially isolated antibody specifically immunoreactive with polypeptide or polynucleotide antigens, and means for detecting the binding of the polynucleotide or polypeptide antigen to the antibody. In one embodiment, the antibody is attached to a solid support. In a specific embodiment, the antibody may be a monoclonal antibody. The detecting means of the kit may include a second, labeled monoclonal antibody. Alternatively, or in addition, the detecting means may include a labeled, competing antigen.

In one diagnostic configuration, test serum is reacted with a solid phase reagent having a surface-bound antigen obtained by the methods of the present invention. After binding with specific antigen antibody to the reagent and removing unbound serum components by washing, the reagent is reacted with reporter-labeled anti-human antibody to bind reporter to the reagent in proportion to the amount of

bound anti-antigen antibody on the solid support. The reagent is again washed to remove unbound labeled antibody, and the amount of reporter associated with the reagent is determined. Typically, the reporter is an enzyme which is detected by incubating the solid phase in the presence of a suitable fluorometric, luminescent or colorimetric substrate (Sigma, St. Louis, MO).

The solid surface reagent in the above assay is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plate or filter material. These attachment methods generally include non-specific adsorption of the protein to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

Thus, the invention provides an assay system or kit for carrying out this diagnostic method. The kit generally includes a support with surface-bound recombinant antigens, and a reporter-labeled anti-human antibody for detecting surface-bound anti-antigen antibody.

Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The pancreatic cancer antigen polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each sequence is specifically targeted to and can hybridize with a particular location on an individual human chromosome, thus each polynucleotide of the present invention can routinely be used as a chromosome marker using techniques known in the art.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably at least 15 bp (e.g., 15-25 bp) from the sequences shown in SEQ ID NO:X, or the complement thereto. Primers can optionally be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, preselection by hybridization to construct chromosome specific-cDNA libraries, and computer mapping techniques (See, e.g., Shuler, Trends Biotechnol 16:456-459 (1998) which is hereby incorporated by reference in its entirety).

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes).

Thus, the present invention also provides a method for chromosomal localization which involves (a) preparing PCR primers from the polynucleotide sequences in Table 3 and SEQ ID NO:X and (b) screening somatic cell hybrids containing individual chromosomes.

The polynucleotides of the present invention would likewise be useful for radiation hybrid mapping, HAPPY mapping, and long range restriction mapping. For a review of these techniques and others known in the art, see, e.g. Dear, "Genome Mapping: A Practical Approach," IRL Press at Oxford University Press, London
5 (1997); Aydin, J. Mol. Med. 77:691-694 (1999); Hacia et al., Mol. Psychiatry 3:483-492 (1998); Herrick et al., Chromosome Res. 7:409-423 (1999); Hamilton et al., Methods Cell Biol. 62:265-280 (2000); and/or Ott, J. Hered. 90:68-70 (1999) each of which is hereby incorporated by reference in its entirety.

Once a polynucleotide has been mapped to a precise chromosomal location,
10 the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library).) Assuming 1 megabase mapping resolution and
15 one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in a polynucleotide of the invention and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as
20 deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required
25 to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using the polynucleotides of the invention. Any of these alterations (altered expression,

chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

Thus, the invention provides a method of detecting increased or decreased expression levels of the pancreatic cancer polynucleotides in affected individuals as compared to unaffected individuals using polynucleotides of the present invention and techniques known in the art, including but not limited to the method described in Example 11. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

Thus, the invention also provides a diagnostic method useful during diagnosis of a pancreas related disorder, including pancreas cancer, involving measuring the expression level of pancreatic cancer polynucleotides in pancreatic tissue or other cells or body fluid from an individual and comparing the measured gene expression level with a standard pancreatic cancer polynucleotide expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a pancreas related disorder.

In still another embodiment, the invention includes a kit for analyzing samples for the presence of proliferative and/or cancerous polynucleotides derived from a test subject. In a general embodiment, the kit includes at least one polynucleotide probe containing a nucleotide sequence that will specifically hybridize with a polynucleotide of the invention and a suitable container. In a specific embodiment, the kit includes two polynucleotide probes defining an internal region of the polynucleotide of the invention, where each probe has one strand containing a 31'-mer-end internal to the region. In a further embodiment, the probes may be useful as primers for polymerase chain reaction amplification.

Where a diagnosis of a pancreas related disorder, including, for example, diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed pancreatic cancer polynucleotide expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

By "measuring the expression level of pancreatic cancer polynucleotides" is intended qualitatively or quantitatively measuring or estimating the level of the pancreatic cancer polypeptide or the level of the mRNA encoding the pancreatic cancer polypeptide in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the pancreatic cancer polypeptide level or mRNA level in a second biological sample). Preferably, the pancreatic cancer polypeptide level or mRNA level in the first biological sample is measured or estimated and compared to a standard pancreatic cancer polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the pancreas related disorder or being determined by averaging levels from a population of individuals not having a pancreas related disorder. As will be appreciated in the art, once a standard pancreatic cancer polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

By "biological sample" is intended any biological sample obtained from an individual, body fluid, cell line, tissue culture, or other source which contains pancreatic cancer polypeptide or the corresponding mRNA. As indicated, biological samples include body fluids (such as bile, lymph, sera, plasma, urine, synovial fluid and spinal fluid) which contain the pancreatic cancer polypeptide, pancreas tissue, and other tissue sources found to express the pancreatic cancer polypeptide. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

The method(s) provided above may preferably be applied in a diagnostic method and/or kits in which polynucleotides and/or polypeptides of the invention are attached to a solid support. In one exemplary method, the support may be a "gene chip" or a "biological chip" as described in US Patents 5,837,832, 5,874,219, and 5,856,174. Further, such a gene chip with pancreatic cancer polynucleotides attached may be used to identify polymorphisms between the pancreatic cancer polynucleotide sequences, with polynucleotides isolated from a test subject. The knowledge of such

polymorphisms (i.e. their location, as well as, their existence) would be beneficial in identifying disease loci for many disorders, such as for example, in neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions, though most preferably in pancreas related proliferative, and/or cancerous diseases and conditions. Such a method is described in US Patents 5,858,659 and 5,856,104. The US Patents referenced supra are hereby incorporated by reference in their entirety herein.

The present invention encompasses pancreatic cancer polynucleotides that are chemically synthesized, or reproduced as peptide nucleic acids (PNA), or according to other methods known in the art. The use of PNAs would serve as the preferred form if the polynucleotides of the invention are incorporated onto a solid support, or gene chip. For the purposes of the present invention, a peptide nucleic acid (PNA) is a polyamide type of DNA analog and the monomeric units for adenine, guanine, thymine and cytosine are available commercially (Perceptive Biosystems). Certain components of DNA, such as phosphorus, phosphorus oxides, or deoxyribose derivatives, are not present in PNAs. As disclosed by P. E. Nielsen, M. Egholm, R. H. Berg and O. Buchardt, Science 254, 1497 (1991); and M. Egholm, O. Buchardt, L. Christensen, C. Behrens, S. M. Freier, D. A. Driver, R. H. Berg, S. K. Kim, B. Norden, and P. E. Nielsen, Nature 365, 666 (1993), PNAs bind specifically and tightly to complementary DNA strands and are not degraded by nucleases. In fact, PNA binds more strongly to DNA than DNA itself does. This is probably because there is no electrostatic repulsion between the two strands, and also the polyamide backbone is more flexible. Because of this, PNA/DNA duplexes bind under a wider range of stringency conditions than DNA/DNA duplexes, making it easier to perform multiplex hybridization. Smaller probes can be used than with DNA due to the strong binding. In addition, it is more likely that single base mismatches can be determined with PNA/DNA hybridization because a single mismatch in a PNA/DNA 15-mer lowers the melting point ($T_{sub.m}$) by 8°-20° C, vs. 4°-16° C for the DNA/DNA 15-mer duplex. Also, the absence of charge groups in PNA means that hybridization can

be done at low ionic strengths and reduce possible interference by salt during the analysis.

The present invention have uses which include, but are not limited to, detecting cancer in mammals. In particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: acute myelogenous leukemias including acute monocytic leukemia, acute myeloblastic leukemia, acute promyelocytic leukemia, acute myelomonocytic leukemia, acute erythroleukemia, acute megakaryocytic leukemia, and acute undifferentiated leukemia, etc.; and chronic myelogenous leukemias including chronic myelomonocytic leukemia, chronic granulocytic leukemia, etc. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

Pathological cell proliferative disorders are often associated with inappropriate activation of proto-oncogenes. (Germann, E. P. et al., "The Etiology of Acute Leukemia: Molecular Genetics and Viral Oncology," in Neoplastic Diseases of the Blood, Vol 1., Wiernik, P. H. et al. eds., 161-182 (1985)). Neoplasias are now believed to result from the qualitative alteration of a normal cellular gene product, or from the quantitative modification of gene expression by insertion into the chromosome of a viral sequence, by chromosomal translocation of a gene to a more actively transcribed region, or by some other mechanism. (Germann et al., supra) It is likely that mutated or altered expression of specific genes is involved in the pathogenesis of some leukemias, among other tissues and cell types. (Germann et al., supra) Indeed, the human counterparts of the oncogenes involved in some animal neoplasias have been amplified or translocated in some cases of human leukemia and carcinoma. (Germann et al., supra)

For example, c-myc expression is highly amplified in the non-lymphocytic leukemia cell line HL-60. When HL-60 cells are chemically induced to stop proliferation, the level of c-myc is found to be downregulated. (International Publication Number WO 91/15580). However, it has been shown that exposure of HL-60 cells to a DNA construct that is complementary to the 5' end of c-myc or c-

myb blocks translation of the corresponding mRNAs which downregulates expression of the c-myc or c-myb proteins and causes arrest of cell proliferation and differentiation of the treated cells. (International Publication Number WO 91/15580; Wickstrom et al., Proc. Natl. Acad. Sci. 85:1028 (1988); Anfossi et al., Proc. Natl. Acad. Sci. 86:3379 (1989)). However, the skilled artisan would appreciate the present invention's usefulness is not limited to treatment of proliferative disorders of hematopoietic cells and tissues. in light of the numerous cells and cell types of varying origins which are known to exhibit proliferative phenotypes.

In addition to the foregoing, a pancreatic cancer antigen polynucleotide can be used to control gene expression through triple helix formation or through antisense DNA or RNA. Antisense techniques are discussed, for example, in Okano, J. Neurochem. 56: 560 (1991); "Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance Lee et al., Nucleic Acids Research 6: 3073 (1979); Cooney et al., Science 241: 456 (1988); and Dervan et al., Science 251: 1360 (1991). Both methods rely on binding of the polynucleotide to a complementary DNA or RNA. For these techniques, preferred polynucleotides are usually oligonucleotides 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. The oligonucleotide described above can also be delivered to cells such that the antisense RNA or DNA may be expressed in vivo to inhibit production of polypeptide of the present invention antigens. Both techniques are effective in model systems. and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease, and in particular, for the treatment of proliferative diseases and/or conditions.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, synovial fluid, amniotic fluid, breast milk, lymph, pulmonary sputum or surfactant, urine, fecal matter, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erich, H., PCR Technology, Freeman

and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic
5 markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to pancreas or pancreatic cancer polynucleotides prepared
10 from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

The polynucleotides of the present invention are also useful as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a
15 biological sample. Similarly, polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In addition, for a number of disorders of the above tissues or cells, significantly higher or lower levels of gene expression of the
20 polynucleotides/polypeptides of the present invention may be detected in certain tissues (e.g., tissues expressing polypeptides and/or polynucleotides of the present invention, pancreas and pancreatic cancer tissues and/or cancerous and/or wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a "standard" gene
25 expression level, i.e., the expression level in healthy tissue from an individual not having the disorder.

Thus, the invention provides a diagnostic method of a disorder, which involves: (a) assaying gene expression level in cells or body fluid of an individual; (b) comparing the gene expression level with a standard gene expression level, whereby

an increase or decrease in the assayed gene expression level compared to the standard expression level is indicative of a disorder.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

Polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays such as, for example, ABC immunoperoxidase (Hsu et al., J. Histochem. Cytochem. 29:577-580 (1981)) or cell type(s) (e.g., immunocytochemistry assays).

Antibodies can be used to assay levels of polypeptides encoded by polynucleotides of the invention in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (^{131}I , ^{125}I , ^{123}I , ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium ($^{115\text{m}}\text{In}$, $^{113\text{m}}\text{In}$, ^{112}In , ^{111}In), and technetium (^{99}Tc , $^{99\text{m}}\text{Tc}$), thallium (^{201}Tl), gallium (^{68}Ga , ^{67}Ga), palladium (^{103}Pd), molybdenum (^{99}Mo), xenon (^{133}Xe), fluorine (^{18}F), ^{153}Sm , ^{177}Lu , ^{159}Gd , ^{149}Pm , ^{140}La , ^{175}Yb , ^{166}Ho , ^{90}Y , ^{47}Sc , ^{186}Re , ^{188}Re , ^{142}Pr , ^{105}Rh , ^{97}Ru ;

luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying levels of polypeptide of the present invention in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, ^{131}I , ^{112}In , $^{99\text{m}}\text{Tc}$, (^{131}I , ^{125}I , ^{123}I , ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium ($^{115\text{m}}\text{In}$, $^{113\text{m}}\text{In}$, ^{112}In , ^{111}In), and technetium (^{99}Tc , $^{99\text{m}}\text{Tc}$), thallium (^{201}Ti), gallium (^{68}Ga , ^{67}Ga), palladium (^{103}Pd), molybdenum (^{99}Mo), xenon (^{133}Xe), fluorine (^{18}F , ^{153}Sm , ^{177}Lu , ^{159}Gd , ^{149}Pm , ^{140}La , ^{175}Yb , ^{166}Ho , ^{90}Y , ^{47}Sc , ^{186}Re , ^{188}Re , ^{142}Pr , ^{105}Rh , ^{97}Ru), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for immune system disorder. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of $^{99\text{m}}\text{Tc}$. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which express the polypeptide encoded by a polynucleotide of the invention. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in *Tumor Imaging: The Radiochemical Detection of Cancer*, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.

By "toxin" is meant one or more compounds that bind and activate endogenous cytotoxic effector systems. radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNase, alpha toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. "Toxin" also includes a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, ^{213}Bi , or other radioisotopes such as, for example, ^{103}Pd , ^{133}Xe , ^{131}I , ^{68}Ge , ^{57}Co , ^{65}Zn , ^{85}Sr , ^{32}P , ^{35}S , ^{90}Y , ^{153}Sm , ^{153}Gd , ^{169}Yb , ^{51}Cr , ^{54}Mn , ^{75}Se , ^{113}Sn , $^{90}\text{Yttrium}$, ^{117}Tin , $^{186}\text{Rhenium}$, $^{166}\text{Holmium}$, and $^{188}\text{Rhenium}$; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

Techniques known in the art may be applied to label polypeptides of the invention (including antibodies). Such techniques include, but are not limited to, the

use of bifunctional conjugating agents (see e.g., U.S. Patent Nos. 5,756,065; 5,714,631; 5,696,239; 5,652,361; 5,505,931; 5,489,425; 5,435,990; 5,428,139; 5,342,604; 5,274,119; 4,994,560; and 5,808,003; the contents of each of which are hereby incorporated by reference in its entirety).

5 Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression level of a pancreatic cancer polypeptide of the present invention in cells or body fluid of an individual, or more preferably, assaying the expression level of a pancreatic cancer polypeptide of the present invention in pancreatic cells or bile of an individual; and (b) comparing the assayed polypeptide
10 expression level with a standard polypeptide expression level, whereby an increase or decrease in the assayed polypeptide expression level compared to the standard expression level is indicative of a disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for
15 detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

 Moreover, pancreatic cancer antigen polypeptides of the present invention can
20 be used to treat or prevent diseases or conditions such as, for example, neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions, preferably proliferative disorders of the pancreas, and/or cancerous disease and
25 conditions. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B, SOD, catalase, DNA repair proteins), to inhibit the activity of a polypeptide (e.g., an oncogene or tumor suppressor), to activate the
30 activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a

membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth inhibition, enhancement of the immune response to proliferative cells or tissues).

5 Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease (as described supra, and elsewhere herein). For example, administration of an antibody directed to a polypeptide of the present invention can bind, and/or neutralize the polypeptide, and/or reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide,
10 such as by binding to a polypeptide bound to a membrane (receptor).

 At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from
15 a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

Gene Therapy Methods

20 Another aspect of the present invention is to gene therapy methods for treating or preventing disorders, diseases and conditions. The gene therapy methods relate to the introduction of nucleic acid (DNA, RNA and antisense DNA or RNA) sequences into an animal to achieve expression of the polypeptide of the present invention. This method requires a polynucleotide which codes for a polypeptide of the present
25 invention operatively linked to a promoter and any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques are known in the art, see, for example, WO90/11092, which is herein incorporated by reference.

 Thus, for example, cells from a patient may be engineered with a
30 polynucleotide (DNA or RNA) comprising a promoter operably linked to a

polynucleotide of the present invention ex vivo, with the engineered cells then being provided to a patient to be treated with the polypeptide of the present invention. Such methods are well-known in the art. For example, see Belldgrun, A., et al., J. Natl. Cancer Inst. 85: 207-216 (1993); Ferrantini, M. et al., Cancer Research 53: 1107-1112 (1993); Ferrantini, M. et al., J. Immunology 153: 4604-4615 (1994); Kaido, T., et al., Int. J. Cancer 60: 221-229 (1995); Ogura, H., et al., Cancer Research 50: 5102-5106 (1990); Santodonato, L., et al., Human Gene Therapy 7:1-10 (1996); Santodonato, L., et al., Gene Therapy 4:1246-1255 (1997); and Zhang, J.-F. et al., Cancer Gene Therapy 3: 31-38 (1996)), which are herein incorporated by reference. In one embodiment, the cells which are engineered are arterial cells. The arterial cells may be reintroduced into the patient through direct injection to the artery, the tissues surrounding the artery, or through catheter injection.

As discussed in more detail below, the polynucleotide constructs can be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, and the like). The polynucleotide constructs may be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

In one embodiment, the polynucleotide of the present invention is delivered as a naked polynucleotide. The term "naked" polynucleotide, DNA or RNA refers to sequences that are free from any delivery vehicle that acts to assist, promote or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotide of the present invention can also be delivered in liposome formulations and lipofectin formulations and the like can be prepared by methods well known to those skilled in the art. Such methods are described, for example, in U.S. Patent Nos. 5,593,972, 5,589,466, and 5,580,859, which are herein incorporated by reference.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Appropriate vectors include pWLNEO,

pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; pSVK3, pBPV, pMSG and pSVL available from Pharmacia; and pEF1/V5, pcDNA3.1. and pRc/CMV2 available from Invitrogen. Other suitable vectors will be readily apparent to the skilled artisan.

5 Any strong promoter known to those skilled in the art can be used for driving the expression of the polynucleotide sequence. Suitable promoters include adenoviral promoters, such as the adenoviral major late promoter; or heterologous promoters, such as the cytomegalovirus (CMV) promoter; the respiratory syncytial virus (RSV) promoter; inducible promoters, such as the MMT promoter, the metallothionein
10 promoter; heat shock promoters; the albumin promoter; the ApoA1 promoter; human globin promoters; viral thymidine kinase promoters, such as the Herpes Simplex thymidine kinase promoter; retroviral LTRs; the b-actin promoter; and human growth hormone promoters. The promoter also may be the native promoter for the polynucleotide of the present invention.

15 Unlike other gene therapy techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

20 The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system. eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular, fluid,
25 mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues. or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for
30 the reasons discussed below. They may be conveniently delivered by injection into the

tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked nucleic acid sequence injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 mg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration.

The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked DNA constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The naked polynucleotides are delivered by any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, and so-called "gene guns". These delivery methods are known in the art.

The constructs may also be delivered with delivery vehicles such as viral sequences, viral particles, liposome formulations, lipofectin, precipitating agents, etc. Such methods of delivery are known in the art.

In certain embodiments, the polynucleotide constructs are complexed in a liposome preparation. Liposomal preparations for use in the instant invention include cationic (positively charged), anionic (negatively charged) and neutral preparations. However, cationic liposomes are particularly preferred because a tight charge

complex can be formed between the cationic liposome and the polyanionic nucleic acid. Cationic liposomes have been shown to mediate intracellular delivery of plasmid DNA (Felgner et al., Proc. Natl. Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference); mRNA (Malone et al., Proc. Natl. Acad. Sci. USA
5 (1989) 86:6077-6081, which is herein incorporated by reference); and purified transcription factors (Debs et al., J. Biol. Chem. (1990) 265:10189-10192, which is herein incorporated by reference), in functional form.

Cationic liposomes are readily available. For example, N[1-2,3-dioleoyloxy)propyl]-N,N,N-triethylammonium (DOTMA) liposomes are
10 particularly useful and are available under the trademark Lipofectin, from GIBCO BRL, Grand Island, N.Y. (See, also, Felgner et al., Proc. Natl Acad. Sci. USA (1987) 84:7413-7416, which is herein incorporated by reference). Other commercially available liposomes include transfectace (DDAB/DOPE) and DOTAP/DOPE (Boehringer).

15 Other cationic liposomes can be prepared from readily available materials using techniques well known in the art. See, e.g. PCT Publication No. WO 90/11092 (which is herein incorporated by reference) for a description of the synthesis of DOTAP (1,2-bis(oleoyloxy)-3-(trimethylammonio)propane) liposomes. Preparation of DOTMA liposomes is explained in the literature, see, e.g., P. Felgner et al., Proc.
20 Natl. Acad. Sci. USA 84:7413-7417, which is herein incorporated by reference. Similar methods can be used to prepare liposomes from other cationic lipid materials.

Similarly, anionic and neutral liposomes are readily available, such as from Avanti Polar Lipids (Birmingham, Ala.), or can be easily prepared using readily available materials. Such materials include phosphatidyl, choline, cholesterol,
25 phosphatidyl ethanolamine, dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), dioleoylphosphatidyl ethanolamine (DOPE), among others. These materials can also be mixed with the DOTMA and DOTAP starting materials in appropriate ratios. Methods for making liposomes using these materials are well known in the art.

For example, commercially dioleoylphosphatidyl choline (DOPC), dioleoylphosphatidyl glycerol (DOPG), and dioleoylphosphatidyl ethanolamine (DOPE) can be used in various combinations to make conventional liposomes, with or without the addition of cholesterol. Thus, for example, DOPG/DOPC vesicles can be prepared by drying 50 mg each of DOPG and DOPC under a stream of nitrogen gas into a sonication vial. The sample is placed under a vacuum pump overnight and is hydrated the following day with deionized water. The sample is then sonicated for 2 hours in a capped vial, using a Heat Systems model 350 sonicator equipped with an inverted cup (bath type) probe at the maximum setting while the bath is circulated at 15EC. Alternatively, negatively charged vesicles can be prepared without sonication to produce multilamellar vesicles or by extrusion through nucleopore membranes to produce unilamellar vesicles of discrete size. Other methods are known and available to those of skill in the art.

The liposomes can comprise multilamellar vesicles (MLVs), small unilamellar vesicles (SUVs), or large unilamellar vesicles (LUVs), with SUVs being preferred. The various liposome-nucleic acid complexes are prepared using methods well known in the art. See, e.g., Straubinger et al., *Methods of Immunology* (1983), 101:512-527, which is herein incorporated by reference. For example, MLVs containing nucleic acid can be prepared by depositing a thin film of phospholipid on the walls of a glass tube and subsequently hydrating with a solution of the material to be encapsulated. SUVs are prepared by extended sonication of MLVs to produce a homogeneous population of unilamellar liposomes. The material to be entrapped is added to a suspension of preformed MLVs and then sonicated. When using liposomes containing cationic lipids, the dried lipid film is resuspended in an appropriate solution such as sterile water or an isotonic buffer solution such as 10 mM Tris/NaCl, sonicated, and then the preformed liposomes are mixed directly with the DNA. The liposome and DNA form a very stable complex due to binding of the positively charged liposomes to the cationic DNA. SUVs find use with small nucleic acid fragments. LUVs are prepared by a number of methods, well known in the art. Commonly used methods include Ca^{2+} -EDTA chelation (Papahadjopoulos et al., *Biochim. Biophys. Acta*

(1975) 394:483; Wilson et al., Cell (1979) 17:77); ether injection (Deamer, D. and Bangham, A., Biochim. Biophys. Acta (1976) 443:629; Ostro et al., Biochem. Biophys. Res. Commun. (1977) 76:836; Fraley et al., Proc. Natl. Acad. Sci. USA (1979) 76:3348); detergent dialysis (Enoch, H. and Strittmatter, P., Proc. Natl. Acad. Sci. USA (1979) 76:145); and reverse-phase evaporation (REV) (Fraley et al., J. Biol. Chem. (1980) 255:10431; Szoka, F. and Papahadjopoulos, D., Proc. Natl. Acad. Sci. USA (1978) 75:145; Schaefer-Ridder et al., Science (1982) 215:166), which are herein incorporated by reference.

Generally, the ratio of DNA to liposomes will be from about 10:1 to about 1:10. Preferably, the ration will be from about 5:1 to about 1:5. More preferably, the ration will be about 3:1 to about 1:3. Still more preferably, the ratio will be about 1:1.

U.S. Patent No. 5,676,954 (which is herein incorporated by reference) reports on the injection of genetic material, complexed with cationic liposomes carriers, into mice. U.S. Patent Nos. 4,897,355, 4,946,787, 5,049,386, 5,459,127, 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide cationic lipids for use in transfecting DNA into cells and mammals. U.S. Patent Nos. 5,589,466, 5,693,622, 5,580,859, 5,703,055, and international publication no. WO 94/9469 (which are herein incorporated by reference) provide methods for delivering DNA-cationic lipid complexes to mammals.

In certain embodiments, cells are engineered, ex vivo or in vivo, using a retroviral particle containing RNA which comprises a sequence encoding a polypeptide of the present invention. Retroviruses from which the retroviral plasmid vectors may be derived include, but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, Rous sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency virus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the PE501, PA317, R-2, R-AM, PA12, T19-14X, VT-

19-17-H2, RCRE, RCRIP, GP+E-86, GP+envAm12, and DAN cell lines as described in Miller, Human Gene Therapy 1:5-14 (1990), which is incorporated herein by reference in its entirety. The vector may transduce the packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and CaPO₄ precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a lipid, and then administered to a host.

The producer cell line generates infectious retroviral vector particles which include polynucleotide encoding a polypeptide of the present invention. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either in vitro or in vivo. The transduced eukaryotic cells will express a polypeptide of the present invention.

In certain other embodiments, cells are engineered, ex vivo or in vivo, with polynucleotide contained in an adenovirus vector. Adenovirus can be manipulated such that it encodes and expresses a polypeptide of the present invention, and at the same time is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. Adenovirus expression is achieved without integration of the viral DNA into the host cell chromosome, thereby alleviating concerns about insertional mutagenesis. Furthermore, adenoviruses have been used as live enteric vaccines for many years with an excellent safety profile (Schwartz, A. R. et al. (1974) Am. Rev. Respir. Dis.109:233-238). Finally, adenovirus mediated gene transfer has been demonstrated in a number of instances including transfer of alpha-1-antitrypsin and CFTR to the lungs of cotton rats (Rosenfeld, M. A. et al. (1991) Science 252:431-434; Rosenfeld et al., (1992) Cell 68:143-155). Furthermore, extensive studies to attempt to establish adenovirus as a causative agent in human cancer were uniformly negative (Green, M. et al. (1979) Proc. Natl. Acad. Sci. USA 76:6606).

Suitable adenoviral vectors useful in the present invention are described, for example, in Kozarsky and Wilson, Curr. Opin. Genet. Devel. 3:499-503 (1993); Rosenfeld et al., Cell 68:143-155 (1992); Engelhardt et al., Human Genet. Ther. 4:759-769 (1993); Yang et al., Nature Genet. 7:362-369 (1994); Wilson et al., Nature

365:691-692 (1993); and U.S. Patent No. 5,652,224, which are herein incorporated by reference. For example, the adenovirus vector Ad2 is useful and can be grown in human 293 cells. These cells contain the E1 region of adenovirus and constitutively express E1a and E1b, which complement the defective adenoviruses by providing the products of the genes deleted from the vector. In addition to Ad2, other varieties of adenovirus (e.g., Ad3, Ad5, and Ad7) are also useful in the present invention.

Preferably, the adenoviruses used in the present invention are replication deficient. Replication deficient adenoviruses require the aid of a helper virus and/or packaging cell line to form infectious particles. The resulting virus is capable of infecting cells and can express a polynucleotide of interest which is operably linked to a promoter, but cannot replicate in most cells. Replication deficient adenoviruses may be deleted in one or more of all or a portion of the following genes: E1a, E1b, E3, E4, E2a, or L1 through L5.

In certain other embodiments, the cells are engineered, ex vivo or in vivo, using an adeno-associated virus (AAV). AAVs are naturally occurring defective viruses that require helper viruses to produce infectious particles (Muzyczka, N., Curr. Topics in Microbiol. Immunol. 158:97 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells. Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate, but space for exogenous DNA is limited to about 4.5 kb. Methods for producing and using such AAVs are known in the art. See, for example, U.S. Patent Nos. 5,139,941, 5,173,414, 5,354,678, 5,436,146, 5,474,935, 5,478,745, and 5,589,377.

For example, an appropriate AAV vector for use in the present invention will include all the sequences necessary for DNA replication, encapsidation, and host-cell integration. The polynucleotide construct is inserted into the AAV vector using standard cloning methods, such as those found in Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (1989). The recombinant AAV vector is then transfected into packaging cells which are infected with a helper virus, using any standard technique, including lipofection, electroporation, calcium phosphate precipitation, etc. Appropriate helper viruses include adenoviruses,

cytomegaloviruses, vaccinia viruses, or herpes viruses. Once the packaging cells are transfected and infected, they will produce infectious AAV viral particles which contain the polynucleotide construct. These viral particles are then used to transduce eukaryotic cells, either ex vivo or in vivo. The transduced cells will contain the polynucleotide construct integrated into its genome, and will express a polypeptide of the invention.

Another method of gene therapy involves operably associating heterologous control regions and endogenous polynucleotide sequences (e.g. encoding a polypeptide of the present invention) via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not normally expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made, using standard techniques known in the art, which contain the promoter with targeting sequences flanking the promoter. Suitable promoters are described herein. The targeting sequence is sufficiently complementary to an endogenous sequence to permit homologous recombination of the promoter-targeting sequence with the endogenous sequence. The targeting sequence will be sufficiently near the 5' end of the desired endogenous polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination.

The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter. The amplified promoter and targeting sequences are digested and ligated together.

The promoter-targeting sequence construct is delivered to the cells, either as naked polynucleotide, or in conjunction with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, whole viruses, lipofection, precipitating agents, etc., described in more detail above. The P promoter-targeting sequence can
5 be delivered by any method, included direct needle injection, intravenous injection, topical administration, catheter infusion, particle accelerators, etc. The methods are described in more detail below.

The promoter-targeting sequence construct is taken up by cells. Homologous recombination between the construct and the endogenous sequence takes place, such
10 that an endogenous sequence is placed under the control of the promoter. The promoter then drives the expression of the endogenous sequence.

Preferably, the polynucleotide encoding a polypeptide of the present invention contains a secretory signal sequence that facilitates secretion of the protein. Typically, the signal sequence is positioned in the coding region of the polynucleotide
15 to be expressed towards or at the 5' end of the coding region. The signal sequence may be homologous or heterologous to the polynucleotide of interest and may be homologous or heterologous to the cells to be transfected. Additionally, the signal sequence may be chemically synthesized using methods known in the art.

Any mode of administration of any of the above-described polynucleotides
20 constructs can be used so long as the mode results in the expression of one or more molecules in an amount sufficient to provide a therapeutic effect. This includes direct needle injection, systemic injection, catheter infusion, biolistic injectors, particle accelerators (i.e., "gene guns"), gelfoam sponge depots, other commercially available depot materials, osmotic pumps (e.g., Alza minipumps), oral or suppositorial solid
25 (tablet or pill) pharmaceutical formulations, and decanting or topical applications during surgery. For example, direct injection of naked calcium phosphate-precipitated plasmid into rat liver and rat spleen or a protein-coated plasmid into the portal vein has resulted in gene expression of the foreign gene in the rat livers (Kaneda et al., Science 243:375 (1989)).

A preferred method of local administration is by direct injection. Preferably, a recombinant molecule of the present invention complexed with a delivery vehicle is administered by direct injection into or locally within the area of arteries. Administration of a composition locally within the area of arteries refers to injecting
5 the composition centimeters and preferably, millimeters within arteries.

Another method of local administration is to contact a polynucleotide construct of the present invention in or around a surgical wound. For example, a patient can undergo surgery and the polynucleotide construct can be coated on the surface of tissue inside the wound or the construct can be injected into areas of tissue
10 inside the wound.

Therapeutic compositions useful in systemic administration, include recombinant molecules of the present invention complexed to a targeted delivery vehicle of the present invention. Suitable delivery vehicles for use with systemic administration comprise liposomes comprising ligands for targeting the vehicle to a
15 particular site.

Preferred methods of systemic administration, include intravenous injection, aerosol, oral and percutaneous (topical) delivery. Intravenous injections can be performed using methods standard in the art. Aerosol delivery can also be performed using methods standard in the art (see, for example, Stribling et al., Proc. Natl. Acad.
20 Sci. USA 189:11277-11281, 1992, which is incorporated herein by reference). Oral delivery can be performed by complexing a polynucleotide construct of the present invention to a carrier capable of withstanding degradation by digestive enzymes in the gut of an animal. Examples of such carriers, include plastic capsules or tablets, such as those known in the art. Topical delivery can be performed by mixing a
25 polynucleotide construct of the present invention with a lipophilic reagent (e.g., DMSO) that is capable of passing into the skin.

Determining an effective amount of substance to be delivered can depend upon a number of factors including, for example, the chemical structure and biological activity of the substance, the age and weight of the animal, the precise
30 condition requiring treatment and its severity, and the route of administration. The

frequency of treatments depends upon a number of factors, such as the amount of polynucleotide constructs administered per dose, as well as the health and history of the subject. The precise amount, number of doses, and timing of doses will be determined by the attending physician or veterinarian.

- 5 Therapeutic compositions of the present invention can be administered to any animal, preferably to mammals and birds. Preferred mammals include humans, dogs, cats, mice, rats, rabbits, sheep, cattle, horses and pigs, with humans being particularly preferred.

10 **Biological Activities**

- Polynucleotides or polypeptides, or agonists or antagonists of the present invention, can be used in assays to test for one or more biological activities. If these polynucleotides or polypeptides, or agonists or antagonists of the present invention, do exhibit activity in a particular assay, it is likely that these molecules may be
15 involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides, and agonists or antagonists could be used to treat the associated disease.

Immune Activity

- 20 A polypeptide or polynucleotide, or agonists or antagonists of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and
25 macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used as a marker or detector of a particular immune
30 system disease or disorder.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. Polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

Moreover, polynucleotides or polypeptides, or agonists or antagonists of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, polynucleotides or polypeptides, or agonists or antagonists of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, polynucleotides or polypeptides, or agonists or antagonists of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of polynucleotides or polypeptides, or agonists or antagonists of the present invention

that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected include, but
5 are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic
10 Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by polynucleotides
15 or polypeptides, or agonists or antagonists of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host
20 disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The administration of polynucleotides or polypeptides, or agonists or antagonists of the present invention that inhibits an immune response,
25 particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, polynucleotides or polypeptides, or agonists or antagonists of the present invention may also be used to modulate inflammation. For example, polynucleotides or polypeptides, or agonists or antagonists of the present invention
30 may inhibit the proliferation and differentiation of cells involved in an inflammatory

response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including chronic prostatitis, granulomatous prostatitis and malacoplakia, inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

Hyperproliferative Disorders

Polynucleotides or polypeptides, or agonists or antagonists of the present invention can be used to treat or detect hyperproliferative disorders, including neoplasms. Polynucleotides or polypeptides, or agonists or antagonists of the present invention may inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, Polynucleotides or polypeptides, or agonists or antagonists of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by Polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to neoplasms located in the: colon, abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstrom's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

One preferred embodiment utilizes polynucleotides of the present invention to inhibit aberrant cellular division, by gene therapy using the present invention, and/or protein fusions or fragments thereof.

Thus, the present invention provides a method for treating cell proliferative disorders by inserting into an abnormally proliferating cell a polynucleotide of the present invention, wherein said polynucleotide represses said expression.

Another embodiment of the present invention provides a method of treating cell-proliferative disorders in individuals comprising administration of one or more active gene copies of the present invention to an abnormally proliferating cell or cells. In a preferred embodiment, polynucleotides of the present invention is a DNA construct comprising a recombinant expression vector effective in expressing a DNA sequence encoding said polynucleotides. In another preferred embodiment of the present invention, the DNA construct encoding the polynucleotides of the present invention is inserted into cells to be treated utilizing a retrovirus, or more preferably an adenoviral vector (See G J. Nabel, et. al., PNAS 1999 96: 324-326, which is hereby incorporated by reference). In a most preferred embodiment, the viral vector is defective and will not transform non-proliferating cells, only proliferating cells. Moreover, in a preferred embodiment, the polynucleotides of the present invention inserted into proliferating cells either alone, or in combination with or fused to other polynucleotides, can then be modulated via an external stimulus (i.e. magnetic, specific small molecule, chemical, or drug administration, etc.), which acts upon the promoter upstream of said polynucleotides to induce expression of the encoded protein product. As such the beneficial therapeutic affect of the present invention

may be expressly modulated (i.e. to increase, decrease, or inhibit expression of the present invention) based upon said external stimulus.

Polynucleotides of the present invention may be useful in repressing expression of oncogenic genes or antigens. By "repressing expression of the oncogenic genes " is intended the suppression of the transcription of the gene, the degradation of the gene transcript (pre-message RNA), the inhibition of splicing, the destruction of the messenger RNA, the prevention of the post-translational modifications of the protein, the destruction of the protein, or the inhibition of the normal function of the protein.

For local administration to abnormally proliferating cells, polynucleotides of the present invention may be administered by any method known to those of skill in the art including, but not limited to transfection, electroporation, microinjection of cells, or in vehicles such as liposomes, lipofectin, or as naked polynucleotides, or any other method described throughout the specification. The polynucleotide of the present invention may be delivered by known gene delivery systems such as, but not limited to, retroviral vectors (Gilboa, J. Virology 44:845 (1982); Hocke, Nature 320:275 (1986); Wilson, et al., Proc. Natl. Acad. Sci. U.S.A. 85:3014), vaccinia virus system (Chakrabarty et al., Mol. Cell Biol. 5:3403 (1985) or other efficient DNA delivery systems (Yates et al., Nature 313:812 (1985)) known to those skilled in the art. These references are exemplary only and are hereby incorporated by reference. In order to specifically deliver or transfect cells which are abnormally proliferating and spare non-dividing cells, it is preferable to utilize a retrovirus, or adenoviral (as described in the art and elsewhere herein) delivery system known to those of skill in the art. Since host DNA replication is required for retroviral DNA to integrate and the retrovirus will be unable to self replicate due to the lack of the retrovirus genes needed for its life cycle. Utilizing such a retroviral delivery system for polynucleotides of the present invention will target said gene and constructs to abnormally proliferating cells and will spare the non-dividing normal cells.

The polynucleotides of the present invention may be delivered directly to cell proliferative disorder/disease sites in internal organs, body cavities and the like by use

of imaging devices used to guide an injecting needle directly to the disease site. The polynucleotides of the present invention may also be administered to disease sites at the time of surgical intervention.

By "cell proliferative disease" is meant any human or animal disease or disorder, affecting any one or any combination of organs, cavities, or body parts, which is characterized by single or multiple local abnormal proliferations of cells, groups of cells, or tissues, whether benign or malignant.

Any amount of the polynucleotides of the present invention may be administered as long as it has a biologically inhibiting effect on the proliferation of the treated cells. Moreover, it is possible to administer more than one of the polynucleotide of the present invention simultaneously to the same site. By "biologically inhibiting" is meant partial or total growth inhibition as well as decreases in the rate of proliferation or growth of the cells. The biologically inhibitory dose may be determined by assessing the effects of the polynucleotides of the present invention on target malignant or abnormally proliferating cell growth in tissue culture, tumor growth in animals and cell cultures, or any other method known to one of ordinary skill in the art.

The present invention is further directed to antibody-based therapies which involve administering of anti-polypeptides and anti-polynucleotide antibodies to a mammalian, preferably human, patient for treating one or more of the described disorders. Methods for producing anti-polypeptides and anti-polynucleotide antibodies polyclonal and monoclonal antibodies are described in detail elsewhere herein. Such antibodies may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of

the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

In particular, the antibodies, fragments and derivatives of the present invention are useful for treating a subject having or developing cell proliferative and/or differentiation disorders as described herein. Such treatment comprises administering
5 a single or multiple doses of the antibody, or a fragment, derivative, or a conjugate thereof.

The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or
10 hematopoietic growth factors, for example., which serve to increase the number or activity of effector cells which interact with the antibodies.

It is preferred to use high affinity and/or potent in vivo inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and
15 therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides, including fragments thereof. Preferred binding affinities include those with a dissociation constant or K_d less than $5 \times 10^{-6}M$, $10^{-6}M$, $5 \times 10^{-7}M$, $10^{-7}M$, $5 \times 10^{-8}M$, $10^{-8}M$, $5 \times 10^{-9}M$, $10^{-9}M$,
20 $5 \times 10^{-10}M$, $10^{-10}M$, $5 \times 10^{-11}M$, $10^{-11}M$, $5 \times 10^{-12}M$, $10^{-12}M$, $5 \times 10^{-13}M$, $10^{-13}M$, $5 \times 10^{-14}M$, $10^{-14}M$, $5 \times 10^{-15}M$, and $10^{-15}M$.

Moreover, polypeptides of the present invention are useful in inhibiting the angiogenesis of proliferative cells or tissues, either alone, as a protein fusion, or in combination with other polypeptides directly or indirectly, as described elsewhere
25 herein. In a most preferred embodiment, said anti-angiogenesis effect may be achieved indirectly, for example, through the inhibition of hematopoietic, tumor-specific cells, such as tumor-associated macrophages (See Joseph IB, et al. J Natl Cancer Inst, 90(21):1648-53 (1998), which is hereby incorporated by reference). Antibodies directed to polypeptides or polynucleotides of the present invention may
30 also result in inhibition of angiogenesis directly, or indirectly (See Witte L, et al.,

Cancer Metastasis Rev. 17(2):155-61 (1998), which is hereby incorporated by reference)).

Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a death-domain receptor, such as tumor necrosis factor (TNF) receptor-1, CD95 (Fas/APO-1), TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1 and -2 (See Schulze-Osthoff K, et.al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides may induce apoptosis through other mechanisms, such as in the activation of other proteins which will activate apoptosis, or through stimulating the expression of said proteins, either alone or in combination with small molecule drugs or adjuvants, such as apoptonin, galectins, thioredoxins, antiinflammatory proteins (See for example, Mutat Res 400(1-2):447-55 (1998), Med Hypotheses.50(5):423-33 (1998), Chem Biol Interact. Apr 24;111-112:23-34 (1998), J Mol Med.76(6):402-12 (1998), Int J Tissue React;20(1):3-15 (1998), which are all hereby incorporated by reference).

Polypeptides, including protein fusions to, or fragments thereof, of the present invention are useful in inhibiting the metastasis of proliferative cells or tissues. Inhibition may occur as a direct result of administering polypeptides, or antibodies directed to said polypeptides as described elsewhere herein, or indirectly, such as activating the expression of proteins known to inhibit metastasis, for example alpha 4 integrins, (See, e.g., Curr Top Microbiol Immunol 1998;231:125-41, which is hereby incorporated by reference). Such therapeutic affects of the present invention may be achieved either alone, or in combination with small molecule drugs or adjuvants.

In another embodiment, the invention provides a method of delivering compositions containing the polypeptides of the invention (e.g., compositions containing polypeptides or polypeptide antibodies associated with heterologous

polypeptides, heterologous nucleic acids, toxins, or prodrugs) to targeted cells expressing the polypeptide of the present invention. Polypeptides or polypeptide antibodies of the invention may be associated with heterologous polypeptides, heterologous nucleic acids, toxins, or prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. Polypeptides, protein fusions to, or fragments thereof, of the present invention are useful in enhancing the immunogenicity and/or antigenicity of proliferating cells or tissues, either directly, such as would occur if the polypeptides of the present invention 'vaccinated' the immune response to respond to proliferative antigens and immunogens, or indirectly, such as in activating the expression of proteins known to enhance the immune response (e.g. chemokines), to said antigens and immunogens.

Cardiovascular Disorders

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, may be used to treat cardiovascular disorders, including peripheral artery disease, such as limb ischemia.

Cardiovascular disorders include cardiovascular abnormalities, such as arterio-arterial fistula, arteriovenous fistula, cerebral arteriovenous malformations, congenital heart defects, pulmonary atresia, and Scimitar Syndrome. Congenital heart defects include aortic coarctation, cor triatriatum, coronary vessel anomalies, crisscross heart, dextrocardia, patent ductus arteriosus, Ebstein's anomaly, Eisenmenger complex, hypoplastic left heart syndrome, levocardia, tetralogy of fallot, transposition of great vessels, double outlet right ventricle, tricuspid atresia, persistent truncus arteriosus, and heart septal defects, such as aortopulmonary septal defect, endocardial cushion defects, Lutembacher's Syndrome, trilogly of Fallot, ventricular heart septal defects.

Cardiovascular disorders also include heart disease, such as arrhythmias, carcinoid heart disease, high cardiac output, low cardiac output, cardiac tamponade, endocarditis (including bacterial), heart aneurysm, cardiac arrest, congestive heart failure, congestive cardiomyopathy, paroxysmal dyspnea, cardiac edema, heart hypertrophy, congestive cardiomyopathy, left ventricular hypertrophy, right

ventricular hypertrophy, post-infarction heart rupture, ventricular septal rupture, heart valve diseases, myocardial diseases, myocardial ischemia, pericardial effusion, pericarditis (including constrictive and tuberculous), pneumopericardium, postpericardiotomy syndrome, pulmonary heart disease, rheumatic heart disease, 5 ventricular dysfunction, hyperemia, cardiovascular pregnancy complications, Scimitar Syndrome, cardiovascular syphilis, and cardiovascular tuberculosis.

Arrhythmias include sinus arrhythmia, atrial fibrillation, atrial flutter, bradycardia, extrasystole, Adams-Stokes Syndrome, bundle-branch block, sinoatrial block, long QT syndrome, parasystole, Lown-Ganong-Levine Syndrome, Mahaim- 10 type pre-excitation syndrome, Wolff-Parkinson-White syndrome, sick sinus syndrome, tachycardias, and ventricular fibrillation. Tachycardias include paroxysmal tachycardia, supraventricular tachycardia, accelerated idioventricular rhythm, atrioventricular nodal reentry tachycardia, ectopic atrial tachycardia, ectopic junctional tachycardia, sinoatrial nodal reentry tachycardia, sinus tachycardia, 15 Torsades de Pointes, and ventricular tachycardia.

Heart valve disease include aortic valve insufficiency, aortic valve stenosis, hear murmurs, aortic valve prolapse, mitral valve prolapse, tricuspid valve prolapse, mitral valve insufficiency, mitral valve stenosis, pulmonary atresia, pulmonary valve insufficiency, pulmonary valve stenosis, tricuspid atresia, tricuspid valve 20 insufficiency, and tricuspid valve stenosis.

Myocardial diseases include alcoholic cardiomyopathy, congestive cardiomyopathy, hypertrophic cardiomyopathy, aortic subvalvular stenosis, pulmonary subvalvular stenosis, restrictive cardiomyopathy, Chagas cardiomyopathy, endocardial fibroelastosis, endomyocardial fibrosis, Kearns Syndrome, myocardial 25 reperfusion injury, and myocarditis.

Myocardial ischemias include coronary disease, such as angina pectoris, coronary aneurysm, coronary arteriosclerosis, coronary thrombosis, coronary vasospasm, myocardial infarction and myocardial stunning.

Cardiovascular diseases also include vascular diseases such as aneurysms, 30 angiodyplasia, angiomatosis, bacillary angiomatosis, Hippel-Lindau Disease,

Klippel-Trenaunay-Weber Syndrome. Sturge-Weber Syndrome. angioneurotic edema, aortic diseases. Takayasu's Arteritis. aortitis. Leriche's Syndrome, arterial occlusive diseases, arteritis, enarteritis, polyarteritis nodosa. cerebrovascular disorders, diabetic angiopathies, diabetic retinopathy, embolisms. thrombosis, erythromelalgia, hemorrhoids, hepatic veno-occlusive disease, hypertension, hypotension, ischemia, peripheral vascular diseases. phlebitis. pulmonary veno-occlusive disease, Raynaud's disease, CREST syndrome, retinal vein occlusion, Scimitar syndrome, superior vena cava syndrome, telangiectasia, atacia telangiectasia, hereditary hemorrhagic telangiectasia, varicocele, varicose veins, varicose ulcer, vasculitis, and venous insufficiency.

Aneurysms include dissecting aneurysms. false aneurysms. infected aneurysms, ruptured aneurysms, aortic aneurysms, cerebral aneurysms, coronary aneurysms, heart aneurysms, and iliac aneurysms.

Arterial occlusive diseases include arteriosclerosis, intermittent claudication, carotid stenosis, fibromuscular dysplasias, mesenteric vascular occlusion, Moyamoya disease, renal artery obstruction, retinal artery occlusion, and thromboangiitis obliterans.

Cerebrovascular disorders include carotid artery diseases, cerebral amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformation, cerebral artery diseases. cerebral embolism and thrombosis, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, cerebral hemorrhage, epidural hematoma, subdural hematoma, subarachnoid hemorrhage, cerebral infarction, cerebral ischemia (including transient), subclavian steal syndrome, periventricular leukomalacia, vascular headache, cluster headache, migraine, and vertebrobasilar insufficiency.

Embolisms include air embolisms, amniotic fluid embolisms, cholesterol embolisms. blue toe syndrome, fat embolisms, pulmonary embolisms, and thromboembolisms. Thrombosis include coronary thrombosis, hepatic vein thrombosis, retinal vein occlusion, carotid artery thrombosis, sinus thrombosis, Wallenberg's syndrome, and thrombophlebitis.

Ischemia includes cerebral ischemia, ischemic colitis, compartment syndromes, anterior compartment syndrome, myocardial ischemia, reperfusion injuries, and peripheral limb ischemia. Vasculitis includes aortitis, arteritis, Behcet's Syndrome, Churg-Strauss Syndrome, mucocutaneous lymph node syndrome, 5 thromboangiitis obliterans, hypersensitivity vasculitis, Schoenlein-Henoch purpura, allergic cutaneous vasculitis, and Wegener's granulomatosis.

Polynucleotides or polypeptides, or agonists or antagonists of the present invention, are especially effective for the treatment of critical limb ischemia and coronary disease.

10 Polypeptides may be administered using any method known in the art, including, but not limited to, direct needle injection at the delivery site, intravenous injection, topical administration, catheter infusion, biolistic injectors, particle accelerators, gelfoam sponge depots, other commercially available depot materials, osmotic pumps, oral or suppositorial solid pharmaceutical formulations, decanting or 15 topical applications during surgery, aerosol delivery. Such methods are known in the art. Polypeptides may be administered as part of a Therapeutic, described in more detail below. Methods of delivering polynucleotides are described in more detail herein.

20 Anti-Angiogenesis Activity

The naturally occurring balance between endogenous stimulators and inhibitors of angiogenesis is one in which inhibitory influences predominate. Rastinejad *et al.*, *Cell* 56:345-355 (1989). In those rare instances in which neovascularization occurs under normal physiological conditions, such as wound 25 healing, organ regeneration, embryonic development, and female reproductive processes, angiogenesis is stringently regulated and spatially and temporally delimited. Under conditions of pathological angiogenesis such as that characterizing solid tumor growth, these regulatory controls fail. Unregulated angiogenesis becomes pathologic and sustains progression of many neoplastic and non-neoplastic diseases. 30 A number of serious diseases are dominated by abnormal neovascularization

including solid tumor growth and metastases, arthritis, some types of eye disorders, and psoriasis. See, e.g., reviews by Moses *et al.*, *Biotech.* 9:630-634 (1991); Folkman *et al.*, *N. Engl. J. Med.*, 333:1757-1763 (1995); Auerbach *et al.*, *J. Microvasc. Res.* 29:401-411 (1985); Folkman, *Advances in Cancer Research*, eds. Klein and Weinhouse. Academic Press, New York, pp. 175-203 (1985); Patz, *Am. J. Ophthalmol.* 94:715-743 (1982); and Folkman *et al.*, *Science* 221:719-725 (1983). In a number of pathological conditions, the process of angiogenesis contributes to the disease state. For example, significant data have accumulated which suggest that the growth of solid tumors is dependent on angiogenesis. Folkman and Klagsbrun, *Science* 235:442-447 (1987).

The polynucleotides encoding a polypeptide of the present invention may be administered along with other polynucleotides encoding an angiogenic protein. Examples of angiogenic proteins include, but are not limited to, acidic and basic fibroblast growth factors, VEGF-1, VEGF-2, VEGF-3, epidermal growth factor alpha and beta, platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor alpha, hepatocyte growth factor, insulin like growth factor, colony stimulating factor, macrophage colony stimulating factor, granulocyte/macrophage colony stimulating factor, and nitric oxide synthase.

The present invention provides for treatment of diseases or disorders associated with neovascularization by administration of the polynucleotides and/or polypeptides of the invention, as well as agonists or antagonists of the present invention. Malignant and metastatic conditions which can be treated with the polynucleotides and polypeptides, or agonists or antagonists of the invention include, but are not limited to, malignancies, solid tumors, and cancers described herein and otherwise known in the art (for a review of such disorders, see Fishman *et al.*, *Medicine*, 2d Ed., J. B. Lippincott Co., Philadelphia (1985)). Thus, the present invention provides a method of treating an angiogenesis-related disease and/or disorder, comprising administering to an individual in need thereof a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist of the invention. For example, polynucleotides, polypeptides, antagonists and/or agonists

may be utilized in a variety of additional methods in order to therapeutically treat a cancer or tumor. Cancers which may be treated with polynucleotides, polypeptides, antagonists and/or agonists include, but are not limited to solid tumors, including pancreas, prostate, lung, breast, ovarian, stomach, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, thyroid cancer; primary tumors and metastases; melanomas; glioblastoma; Kaposi's sarcoma; leiomyosarcoma; non-small cell lung cancer; colorectal cancer; advanced malignancies; and blood born tumors such as leukemias. For example, polynucleotides, polypeptides, antagonists and/or agonists may be delivered topically, in order to treat cancers such as skin cancer, head and neck tumors, breast tumors, and Kaposi's sarcoma.

Within yet other aspects, polynucleotides, polypeptides, antagonists and/or agonists may be utilized to treat superficial forms of bladder cancer by, for example, intravesical administration. Polynucleotides, polypeptides, antagonists and/or agonists may be delivered directly into the tumor, or near the tumor site, via injection or a catheter. Of course, as the artisan of ordinary skill will appreciate, the appropriate mode of administration will vary according to the cancer to be treated. Other modes of delivery are discussed herein.

Polynucleotides, polypeptides, antagonists and/or agonists may be useful in treating other disorders, besides cancers, which involve angiogenesis. These disorders include, but are not limited to: benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization;

telangiectasia; hemophiliac joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis.

For example, within one aspect of the present invention methods are provided for treating hypertrophic scars and keloids, comprising the step of administering a polynucleotide, polypeptide, antagonist and/or agonist of the invention to a hypertrophic scar or keloid.

Within one embodiment of the present invention polynucleotides, polypeptides, antagonists and/or agonists are directly injected into a hypertrophic scar or keloid, in order to prevent the progression of these lesions. This therapy is of particular value in the prophylactic treatment of conditions which are known to result in the development of hypertrophic scars and keloids (e.g., burns), and is preferably initiated after the proliferative phase has had time to progress (approximately 14 days after the initial injury), but before hypertrophic scar or keloid development. As noted above, the present invention also provides methods for treating neovascular diseases of the eye, including for example, corneal neovascularization, neovascular glaucoma, proliferative diabetic retinopathy, retrolental fibroplasia and macular degeneration.

Moreover, Ocular disorders associated with neovascularization which can be treated with the polynucleotides and polypeptides of the present invention (including agonists and/or antagonists) include, but are not limited to: neovascular glaucoma, diabetic retinopathy, retinoblastoma, retrolental fibroplasia, uveitis, retinopathy of prematurity macular degeneration, corneal graft neovascularization, as well as other eye inflammatory diseases, ocular tumors and diseases associated with choroidal or iris neovascularization. See, e.g., reviews by Waltman *et al.*, *Am. J. Ophthalmol.* 85:704-710 (1978) and Gartner *et al.*, *Surv. Ophthalmol.* 22:291-312 (1978).

Thus, within one aspect of the present invention methods are provided for treating neovascular diseases of the eye such as corneal neovascularization (including corneal graft neovascularization), comprising the step of administering to a patient a therapeutically effective amount of a compound (as described above) to the cornea, such that the formation of blood vessels is inhibited. Briefly, the cornea is a tissue which normally lacks blood vessels. In certain pathological conditions however,

capillaries may extend into the cornea from the pericorneal vascular plexus of the limbus. When the cornea becomes vascularized, it also becomes clouded, resulting in a decline in the patient's visual acuity. Visual loss may become complete if the cornea completely opacitates. A wide variety of disorders can result in corneal neovascularization, including for example, corneal infections (e.g., trachoma, herpes simplex keratitis, leishmaniasis and onchocerciasis), immunological processes (e.g., graft rejection and Stevens-Johnson's syndrome), alkali burns, trauma, inflammation (of any cause), toxic and nutritional deficiency states, and as a complication of wearing contact lenses.

10 Within particularly preferred embodiments of the invention, may be prepared for topical administration in saline (combined with any of the preservatives and antimicrobial agents commonly used in ocular preparations), and administered in eyedrop form. The solution or suspension may be prepared in its pure form and administered several times daily. Alternatively, anti-angiogenic compositions, 15 prepared as described above, may also be administered directly to the cornea. Within preferred embodiments, the anti-angiogenic composition is prepared with a muco-adhesive polymer which binds to cornea. Within further embodiments, the anti-angiogenic factors or anti-angiogenic compositions may be utilized as an adjunct to conventional steroid therapy. Topical therapy may also be useful prophylactically in 20 corneal lesions which are known to have a high probability of inducing an angiogenic response (such as chemical burns). In these instances the treatment, likely in combination with steroids, may be instituted immediately to help prevent subsequent complications.

 Within other embodiments, the compounds described above may be injected 25 directly into the corneal stroma by an ophthalmologist under microscopic guidance. The preferred site of injection may vary with the morphology of the individual lesion, but the goal of the administration would be to place the composition at the advancing front of the vasculature (i.e., interspersed between the blood vessels and the normal cornea). In most cases this would involve perilimbal corneal injection to "protect" the 30 cornea from the advancing blood vessels. This method may also be utilized shortly

after a corneal insult in order to prophylactically prevent corneal neovascularization. In this situation the material could be injected in the perilimbic cornea interspersed between the corneal lesion and its undesired potential limbic blood supply. Such methods may also be utilized in a similar fashion to prevent capillary invasion of transplanted corneas. In a sustained-release form injections might only be required 2-3 times per year. A steroid could also be added to the injection solution to reduce inflammation resulting from the injection itself.

Within another aspect of the present invention, methods are provided for treating neovascular glaucoma, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. In one embodiment, the compound may be administered topically to the eye in order to treat early forms of neovascular glaucoma. Within other embodiments, the compound may be implanted by injection into the region of the anterior chamber angle. Within other embodiments, the compound may also be placed in any location such that the compound is continuously released into the aqueous humor. Within another aspect of the present invention, methods are provided for treating proliferative diabetic retinopathy, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eyes, such that the formation of blood vessels is inhibited.

Within particularly preferred embodiments of the invention, proliferative diabetic retinopathy may be treated by injection into the aqueous humor or the vitreous, in order to increase the local concentration of the polynucleotide, polypeptide, antagonist and/or agonist in the retina. Preferably, this treatment should be initiated prior to the acquisition of severe disease requiring photocoagulation.

Within another aspect of the present invention, methods are provided for treating retrolental fibroplasia, comprising the step of administering to a patient a therapeutically effective amount of a polynucleotide, polypeptide, antagonist and/or agonist to the eye, such that the formation of blood vessels is inhibited. The

compound may be administered topically, via intravitreal injection and/or via intraocular implants.

Additionally, disorders which can be treated with the polynucleotides, polypeptides, agonists and/or antagonists include, but are not limited to, hemangioma, arthritis, psoriasis, angiofibroma, atherosclerotic plaques, delayed wound healing, 5 granulations, hemophilic joints, hypertrophic scars, nonunion fractures, Osler-Weber syndrome, pyogenic granuloma, scleroderma, trachoma, and vascular adhesions.

Moreover, disorders and/or states, which can be treated with the polynucleotides, polypeptides, agonists and/or antagonists include, but are not limited to, solid tumors, blood born tumors such as leukemias, tumor metastasis, 10 Kaposi's sarcoma, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas, rheumatoid arthritis, psoriasis, ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, and uveitis, delayed wound healing, 15 endometriosis, vasculogenesis, granulations, hypertrophic scars (keloids), nonunion fractures, scleroderma, trachoma, vascular adhesions, myocardial angiogenesis, coronary collaterals, cerebral collaterals, arteriovenous malformations, ischemic limb angiogenesis, Osler-Webber Syndrome, plaque neovascularization, telangiectasia, 20 hemophilic joints, angiofibroma fibromuscular dysplasia, wound granulation, Crohn's disease, atherosclerosis, birth control agent by preventing vascularization required for embryo implantation controlling menstruation, diseases that have angiogenesis as a pathologic consequence such as cat scratch disease (Rochelie minalia quintosa), ulcers (*Helicobacter pylori*), Bartonellosis and bacillary 25 angiomatosis.

In one aspect of the birth control method, an amount of the compound sufficient to block embryo implantation is administered before or after intercourse and fertilization have occurred, thus providing an effective method of birth control, possibly a "morning after" method. Polynucleotides, polypeptides, agonists and/or 30 antagonists may also be used in controlling menstruation or administered as either a

peritoneal lavage fluid or for peritoneal implantation in the treatment of endometriosis.

Polynucleotides, polypeptides, agonists and/or agonists of the present invention may be incorporated into surgical sutures in order to prevent stitch
5 granulomas.

Polynucleotides, polypeptides, agonists and/or agonists may be utilized in a wide variety of surgical procedures. For example, within one aspect of the present invention a compositions (in the form of, for example, a spray or film) may be utilized to coat or spray an area prior to removal of a tumor, in order to isolate normal
10 surrounding tissues from malignant tissue, and/or to prevent the spread of disease to surrounding tissues. Within other aspects of the present invention, compositions (e.g., in the form of a spray) may be delivered via endoscopic procedures in order to coat tumors, or inhibit angiogenesis in a desired locale. Within yet other aspects of the present invention, surgical meshes which have been coated with anti- angiogenic
15 compositions of the present invention may be utilized in any procedure wherein a surgical mesh might be utilized. For example, within one embodiment of the invention a surgical mesh laden with an anti-angiogenic composition may be utilized during abdominal cancer resection surgery (e.g., subsequent to colon resection) in order to provide support to the structure, and to release an amount of the anti-
20 angiogenic factor.

Within further aspects of the present invention, methods are provided for treating tumor excision sites, comprising administering a polynucleotide, polypeptide, agonist and/or agonist to the resection margins of a tumor subsequent to excision, such that the local recurrence of cancer and the formation of new blood vessels at the
25 site is inhibited. Within one embodiment of the invention, the anti-angiogenic compound is administered directly to the tumor excision site (e.g., applied by swabbing, brushing or otherwise coating the resection margins of the tumor with the anti-angiogenic compound). Alternatively, the anti-angiogenic compounds may be incorporated into known surgical pastes prior to administration. Within particularly

preferred embodiments of the invention, the anti-angiogenic compounds are applied after hepatic resections for malignancy, and after neurosurgical operations.

Within one aspect of the present invention, polynucleotides, polypeptides, agonists and/or agonists may be administered to the resection margin of a wide variety of tumors, including for example, breast, colon, brain and hepatic tumors. For example, within one embodiment of the invention, anti-angiogenic compounds may be administered to the site of a neurological tumor subsequent to excision, such that the formation of new blood vessels at the site are inhibited.

The polynucleotides, polypeptides, agonists and/or agonists of the present invention may also be administered along with other anti-angiogenic factors. Representative examples of other anti-angiogenic factors include: Anti-Invasive Factor, retinoic acid and derivatives thereof, paclitaxel, Suramin, Tissue Inhibitor of Metalloproteinase-1, Tissue Inhibitor of Metalloproteinase-2, Plasminogen Activator Inhibitor-1, Plasminogen Activator Inhibitor-2, and various forms of the lighter "d group" transition metals.

Lighter "d group" transition metals include, for example, vanadium, molybdenum, tungsten, titanium, niobium, and tantalum species. Such transition metal species may form transition metal complexes. Suitable complexes of the above-mentioned transition metal species include oxo transition metal complexes.

Representative examples of vanadium complexes include oxo vanadium complexes such as vanadate and vanadyl complexes. Suitable vanadate complexes include metavanadate and orthovanadate complexes such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

Representative examples of tungsten and molybdenum complexes also include oxo complexes. Suitable oxo tungsten complexes include tungstate and tungsten oxide complexes. Suitable tungstate complexes include ammonium tungstate, calcium tungstate, sodium tungstate dihydrate, and tungstic acid. Suitable tungsten oxides include tungsten (IV) oxide and tungsten (VI) oxide. Suitable oxo

molybdenum complexes include molybdate, molybdenum oxide, and molybdenyl complexes. Suitable molybdate complexes include ammonium molybdate and its hydrates, sodium molybdate and its hydrates, and potassium molybdate and its hydrates. Suitable molybdenum oxides include molybdenum (VI) oxide, molybdenum (VI) oxide, and molybdic acid. Suitable molybdenyl complexes include, for example, molybdenyl acetylacetonate. Other suitable tungsten and molybdenum complexes include hydroxo derivatives derived from, for example, glycerol, tartaric acid, and sugars.

A wide variety of other anti-angiogenic factors may also be utilized within the context of the present invention. Representative examples include platelet factor 4; protamine sulphate; sulphated chitin derivatives (prepared from queen crab shells), (Murata et al., Cancer Res. 51:22-26, 1991); Sulphated Polysaccharide Peptidoglycan Complex (SP- PG) (the function of this compound may be enhanced by the presence of steroids such as estrogen, and tamoxifen citrate); Staurosporine; modulators of matrix metabolism, including for example, proline analogs, cishydroxyproline, d,L-3,4-dehydroproline, Thiaproline, alpha,alpha-dipyridyl, aminopropionitrile fumarate; 4-propyl-5-(4-pyridinyl)-2(3H)-oxazolone; Methotrexate; Mitoxantrone; Heparin; Interferons; 2 Macroglobulin-serum; ChIMP-3 (Pavloff et al., J. Bio. Chem. 267:17321-17326, 1992); Chymostatin (Tomkinson et al., Biochem J. 286:475-480, 1992); Cyclodextrin Tetradecasulfate; Eponemycin; Camptothecin; Fumagillin (Ingber et al., Nature 348:555-557, 1990); Gold Sodium Thiomalate ("GST"; Matsubara and Ziff, J. Clin. Invest. 79:1440-1446, 1987); anticollagenase-serum; alpha2-antiplasmin (Holmes et al., J. Biol. Chem. 262(4):1659-1664, 1987); Bisantrone (National Cancer Institute); Lobenzarit disodium (N-(2)-carboxyphenyl-4-chloroanthronilic acid disodium or "CCA"; Takeuchi et al., Agents Actions 36:312-316, 1992); Thalidomide; Angostatic steroid; AGM-1470; carboxynaminolmidazole; and metalloproteinase inhibitors such as BB94.

Diseases at the Cellular Level

Diseases associated with increased cell survival or the inhibition of apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as antagonists or agonists of the present invention, include cancers (such as follicular lymphomas, carcinomas with p53 mutations, and hormone-dependent tumors, including, but not limited to colon cancer, cardiac tumors, pancreatic cancer, melanoma, retinoblastoma, glioblastoma, lung cancer, intestinal cancer, testicular cancer, stomach cancer, neuroblastoma, myxoma, myoma, lymphoma, endothelioma, osteoblastoma, osteoclastoma, osteosarcoma, chondrosarcoma, adenoma, breast cancer, prostate cancer, Kaposi's sarcoma and ovarian cancer); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) and viral infections (such as herpes viruses, pox viruses and adenoviruses), inflammation, graft v. host disease, acute graft rejection, and chronic graft rejection. In preferred embodiments, polynucleotides, polypeptides, and/or antagonists of the invention are used to inhibit growth, progression, and/or metasis of cancers, in particular those listed above.

Additional diseases or conditions associated with increased cell survival that could be treated or detected by polynucleotides or polypeptides, or agonists or antagonists of the present invention include, but are not limited to, progression, and/or metastases of malignancies and related disorders such as leukemia (including acute leukemias (e.g., acute lymphocytic leukemia, acute myelocytic leukemia (including myeloblastic, promyelocytic, myelomonocytic, monocytic, and erythroleukemia)) and chronic leukemias (e.g., chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia)), polycythemia vera, lymphomas (e.g., Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, heavy chain disease, and solid tumors including, but not limited to, sarcomas and carcinomas such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma,

lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, menangioma, melanoma, neuroblastoma, and retinoblastoma.

Diseases associated with increased apoptosis that could be treated or detected by polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, include AIDS; neurodegenerative disorders (such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, Retinitis pigmentosa, Cerebellar degeneration and brain tumor or prior associated disease); autoimmune disorders (such as, multiple sclerosis, Sjogren's syndrome, Hashimoto's thyroiditis, biliary cirrhosis, Behcet's disease, Crohn's disease, polymyositis, systemic lupus erythematosus and immune-related glomerulonephritis and rheumatoid arthritis) myelodysplastic syndromes (such as aplastic anemia), graft v. host disease, ischemic injury (such as that caused by myocardial infarction, stroke and reperfusion injury), liver injury (e.g., hepatitis related liver injury, ischemia/reperfusion injury, cholestosis (bile duct injury) and liver cancer); toxin-induced liver disease (such as that caused by alcohol), septic shock, cachexia and anorexia.

25

Wound Healing and Epithelial Cell Proliferation

In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to stimulate epithelial cell proliferation and basal keratinocytes for the purpose of wound

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healing, and to stimulate hair follicle production and healing of dermal wounds. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may be clinically useful in stimulating wound healing including surgical wounds, excisional wounds, deep wounds involving damage of the dermis and epidermis, eye tissue wounds, dental tissue wounds, oral cavity wounds, diabetic ulcers, dermal ulcers, cubitus ulcers, arterial ulcers, venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote dermal reestablishment subsequent to dermal loss

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to increase the adherence of skin grafts to a wound bed and to stimulate re-epithelialization from the wound bed. The following are types of grafts that polynucleotides or polypeptides, agonists or antagonists of the present invention, could be used to increase adherence to a wound bed: autografts, artificial skin, allografts, autodermic graft, autoepidermic grafts, avascular grafts, Blair-Brown grafts, bone graft, brephoplastic grafts, cutis graft, delayed graft, dermic graft, epidermic graft, fascia graft, full thickness graft, heterologous graft, xenograft, homologous graft, hyperplastic graft, lamellar graft, mesh graft, mucosal graft, Ollier-Thiersch graft, omentopial graft, patch graft, pedicle graft, penetrating graft, split skin graft, thick split graft. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, can be used to promote skin strength and to improve the appearance of aged skin.

It is believed that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, will also produce changes in hepatocyte proliferation, and epithelial cell proliferation in the lung, breast, pancreas, stomach, small intestine, and large intestine. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could promote proliferation of

epithelial cells such as sebocytes, hair follicles, hepatocytes, type II pneumocytes, mucin-producing goblet cells, and other epithelial cells and their progenitors contained within the skin, lung, liver, and gastrointestinal tract. Polynucleotides or polypeptides, agonists or antagonists of the present invention, may promote
5 proliferation of endothelial cells, keratinocytes, and basal keratinocytes.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to reduce the side effects of gut toxicity that result from radiation, chemotherapy treatments or viral infections. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may have a
10 cytoprotective effect on the small intestine mucosa. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, may also stimulate healing of mucositis (mouth ulcers) that result from chemotherapy and viral infections.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could further be used in full regeneration of skin in full and partial
15 thickness skin defects, including burns, (i.e., repopulation of hair follicles, sweat glands, and sebaceous glands), treatment of other skin defects such as psoriasis. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat epidermolysis bullosa, a defect in adherence of the epidermis to the underlying dermis which results in frequent, open and painful blisters
20 by accelerating reepithelialization of these lesions. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could also be used to treat gastric and duodenal ulcers and help heal by scar formation of the mucosal lining and regeneration of glandular mucosa and duodenal mucosal lining more rapidly. Inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, are
25 diseases which result in destruction of the mucosal surface of the small or large intestine, respectively. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to promote the resurfacing of the mucosal surface to aid more rapid healing and to prevent progression of inflammatory bowel disease. Treatment with polynucleotides or polypeptides, agonists or
30 antagonists of the present invention, is expected to have a significant effect on the

production of mucus throughout the gastrointestinal tract and could be used to protect the intestinal mucosa from injurious substances that are ingested or following surgery. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to treat diseases associate with the under expression.

5 Moreover, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to prevent and heal damage to the lungs due to various pathological states. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, which could stimulate proliferation and differentiation and promote the repair of alveoli and bronchiolar epithelium to prevent
10 or treat acute or chronic lung damage. For example, emphysema, which results in the progressive loss of aveoli, and inhalation injuries. i.e., resulting from smoke inhalation and burns, that cause necrosis of the bronchiolar epithelium and alveoli could be effectively treated using polynucleotides or polypeptides, agonists or antagonists of the present invention. Also, polynucleotides or polypeptides, as well as
15 agonists or antagonists of the present invention, could be used to stimulate the proliferation of and differentiation of type II pneumocytes, which may help treat or prevent disease such as hyaline membrane diseases, such as infant respiratory distress syndrome and bronchopulmonary dislasia, in premature infants.

 Polynucleotides or polypeptides, as well as agonists or antagonists of the
20 present invention, could stimulate the proliferation and differentiation of hepatocytes and, thus, could be used to alleviate or treat liver diseases and pathologies such as fulminant liver failure caused by cirrhosis, liver damage caused by viral hepatitis and toxic substances (i.e., acetaminophen, carbon tetraholoride and other hepatotoxins known in the art).

25 In addition, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used treat or prevent the onset of diabetes mellitus. In patients with newly diagnosed Types I and II diabetes, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could be used to maintain the islet function so as to alleviate,
30 delay or prevent permanent manifestation of the disease. Also, polynucleotides or

polypeptides, as well as agonists or antagonists of the present invention, could be used as an auxiliary in islet cell transplantation to improve or promote islet cell function.

5 Neurological Diseases

In accordance with yet a further aspect of the present invention, there is provided a process for utilizing polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, for therapeutic purposes, for example, to
10 stimulate neurological cell proliferation and/or differentiation. Therefore, polynucleotides, polypeptides, agonists and/or antagonists of the invention may be used to treat and/or detect neurologic diseases. Moreover, polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used as a marker or detector of a particular nervous system disease or disorder.

15 Examples of neurologic diseases which can be treated or detected with polynucleotides, polypeptides, agonists, and/or antagonists of the present invention include brain diseases, such as metabolic brain diseases which includes phenylketonuria such as maternal phenylketonuria, pyruvate carboxylase deficiency, pyruvate dehydrogenase complex deficiency, Wernicke's Encephalopathy, brain
20 edema, brain neoplasms such as cerebellar neoplasms which include infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms, supratentorial neoplasms, canavan disease, cerebellar diseases such as cerebellar ataxia which include spinocerebellar degeneration such as ataxia telangiectasia, cerebellar dyssynergia, Friederich's Ataxia, Machado-Joseph
25 Disease, olivopontocerebellar atrophy, cerebellar neoplasms such as infratentorial neoplasms, diffuse cerebral sclerosis such as encephalitis periaxialis, globoid cell leukodystrophy, metachromatic leukodystrophy and subacute sclerosing panencephalitis, cerebrovascular disorders (such as carotid artery diseases which include carotid artery thrombosis, carotid stenosis and Moyamoya Disease, cerebral
30 amyloid angiopathy, cerebral aneurysm, cerebral anoxia, cerebral arteriosclerosis, cerebral arteriovenous malformations, cerebral artery diseases, cerebral embolism and

thrombosis such as carotid artery thrombosis, sinus thrombosis and Wallenberg's Syndrome, cerebral hemorrhage such as epidural hematoma, subdural hematoma and subarachnoid hemorrhage, cerebral infarction, cerebral ischemia such as transient cerebral ischemia, Subclavian Steal Syndrome and vertebrobasilar insufficiency, 5 vascular dementia such as multi-infarct dementia, periventricular leukomalacia, vascular headache such as cluster headache, migraine, dementia such as AIDS Dementia Complex, presenile dementia such as Alzheimer's Disease and Creutzfeldt-Jakob Syndrome, senile dementia such as Alzheimer's Disease and progressive supranuclear palsy, vascular dementia such as multi-infarct dementia, encephalitis 10 which include encephalitis periaxialis, viral encephalitis such as epidemic encephalitis, Japanese Encephalitis, St. Louis Encephalitis, tick-borne encephalitis and West Nile Fever, acute disseminated encephalomyelitis, meningoencephalitis such as uveomeningoencephalitic syndrome, Postencephalitic Parkinson Disease and subacute sclerosing panencephalitis, encephalomalacia such as periventricular 15 leukomalacia, epilepsy such as generalized epilepsy which includes infantile spasms, absence epilepsy, myoclonic epilepsy which includes MERRF Syndrome, tonic-clonic epilepsy, partial epilepsy such as complex partial epilepsy, frontal lobe epilepsy and temporal lobe epilepsy, post-traumatic epilepsy, status epilepticus such as Epilepsia Partialis Continua, Hallervorden-Spatz Syndrome, hydrocephalus such as 20 Dandy-Walker Syndrome and normal pressure hydrocephalus, hypothalamic diseases such as hypothalamic neoplasms, cerebral malaria, narcolepsy which includes cataplexy, bulbar poliomyelitis, cerebri pseudotumor, Rett Syndrome, Reye's Syndrome, thalamic diseases, cerebral toxoplasmosis, intracranial tuberculoma and Zellweger Syndrome, central nervous system infections such as AIDS Dementia 25 Complex, Brain Abscess, subdural empyema, encephalomyelitis such as Equine Encephalomyelitis, Venezuelan Equine Encephalomyelitis, Necrotizing Hemorrhagic Encephalomyelitis, Visna, cerebral malaria, meningitis such as arachnoiditis, aseptic meningitis such as viral meningitis which includes lymphocytic choriomeningitis. Bacterial meningitis which includes Haemophilus Meningitis, Listeria Meningitis, 30 Meningococcal Meningitis such as Waterhouse-Friderichsen Syndrome,

Pneumococcal Meningitis and meningeal tuberculosis. fungal meningitis such as Cryptococcal Meningitis. subdural effusion. meningoencephalitis such as uvemeningoencephalitic syndrome, myelitis such as transverse myelitis, neurosyphilis such as tabes dorsalis, poliomyelitis which includes bulbar poliomyelitis and postpoliomyelitis syndrome, prion diseases (such as Creutzfeldt-Jakob Syndrome, Bovine Spongiform Encephalopathy, Gerstmann-Straussler Syndrome, Kuru, Scrapie) cerebral toxoplasmosis, central nervous system neoplasms such as brain neoplasms that include cerebellar neoplasms such as infratentorial neoplasms, cerebral ventricle neoplasms such as choroid plexus neoplasms, hypothalamic neoplasms and supratentorial neoplasms. meningeal neoplasms, spinal cord neoplasms which include epidural neoplasms, demyelinating diseases such as Canavan Diseases, diffuse cerebral scleritis which includes adrenoleukodystrophy, encephalitis periaxialis, globoid cell leukodystrophy, diffuse cerebral sclerosis such as metachromatic leukodystrophy, allergic encephalomyelitis, necrotizing hemorrhagic encephalomyelitis, progressive multifocal leukoencephalopathy, multiple sclerosis, central pontine myelinolysis, transverse myelitis, neuromyelitis optica, Scrapie, Swayback, Chronic Fatigue Syndrome, Visna, High Pressure Nervous Syndrome, Meningism, spinal cord diseases such as amyotonia congenita, amyotrophic lateral sclerosis. spinal muscular atrophy such as Werdnig-Hoffmann Disease, spinal cord compression, spinal cord neoplasms such as epidural neoplasms, syringomyelia, Tabes Dorsalis, Stiff-Man Syndrome, mental retardation such as Angelman Syndrome, Cri-du-Chat Syndrome, De Lange's Syndrome, Down Syndrome, Gangliosidoses such as gangliosidoses G(M1), Sandhoff Disease, Tay-Sachs Disease, Hartnup Disease, homocystinuria, Laurence-Moon- Biedl Syndrome, Lesch-Nyhan Syndrome, Maple Syrup Urine Disease, mucopolipidosis such as fucosidosis, neuronal ceroid-lipofuscinosis, oculocerebrorenal syndrome. phenylketonuria such as maternal phenylketonuria, Prader-Willi Syndrome, Rett Syndrome, Rubinstein-Taybi Syndrome, Tuberous Sclerosis, WAGR Syndrome, nervous system abnormalities such as holoprosencephaly, neural tube defects such as anencephaly which includes hydrangencephaly, Arnold-Chairi Deformity, encephalocele. meningocele,

meningomyelocele. spinal dysraphism such as spina bifida cystica and spina bifida occulta. hereditary motor and sensory neuropathies which include Charcot-Marie Disease, Hereditary optic atrophy, Refsum's Disease. hereditary spastic paraplegia, Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies such as Congenital Analgesia and Familial Dysautonomia. Neurologic manifestations (such as agnosia that include Gerstmann's Syndrome. Amnesia such as retrograde amnesia. apraxia, neurogenic bladder, cataplexy, communicative disorders such as hearing disorders that includes deafness, partial hearing loss, loudness recruitment and tinnitus, language disorders such as aphasia which include agraphia, anomia, broca aphasia, and Wernicke Aphasia, Dyslexia such as Acquired Dyslexia, language development disorders, speech disorders such as aphasia which includes anomia, broca aphasia and Wernicke Aphasia. articulation disorders, communicative disorders such as speech disorders which include dysarthria, echolalia, mutism and stuttering, voice disorders such as aphonia and hoarseness, decerebrate state, delirium, fasciculation, hallucinations, meningism, movement disorders such as angelman syndrome, ataxia, athetosis, chorea, dystonia, hypokinesia, muscle hypotonia, myoclonus, tic, torticollis and tremor, muscle hypertonia such as muscle rigidity such as stiff-man syndrome, muscle spasticity, paralysis such as facial paralysis which includes Herpes Zoster Oticus, Gastroparesis, Hemiplegia, ophthalmoplegia such as diplopia, Duane's Syndrome, Horner's Syndrome, Chronic progressive external ophthalmoplegia such as Kearns Syndrome, Bulbar Paralysis, Tropical Spastic Paraparesis, Paraplegia such as Brown-Sequard Syndrome, quadriplegia, respiratory paralysis and vocal cord paralysis, paresis, phantom limb, taste disorders such as ageusia and dysgeusia, vision disorders such as amblyopia, blindness, color vision defects, diplopia, hemianopsia, scotoma and subnormal vision, sleep disorders such as hypersomnia which includes Kleine-Levin Syndrome, insomnia, and somnambulism, spasm such as trismus, unconsciousness such as coma, persistent vegetative state and syncope and vertigo, neuromuscular diseases such as amyotonia congenita, amyotrophic lateral sclerosis, Lambert-Eaton Myasthenic Syndrome, motor neuron disease. muscular atrophy such as spinal muscular atrophy, Charcot-Marie Disease

and Werdnig-Hoffmann Disease. Postpoliomyelitis Syndrome. Muscular Dystrophy, Myasthenia Gravis, Myotonia Atrophica. Myotonia Confenita. Nemaline Myopathy, Familial Periodic Paralysis. Multiplex Paramyoclonus. Tropical Spastic Paraparesis and Stiff-Man Syndrome, peripheral nervous system diseases such as acrodynia, amyloid neuropathies, autonomic nervous system diseases such as Adie's Syndrome, Barre-Lieou Syndrome, Familial Dysautonomia, Horner's Syndrome, Reflex Sympathetic Dystrophy and Shy-Drager Syndrome, Cranial Nerve Diseases such as Acoustic Nerve Diseases such as Acoustic Neuroma which includes Neurofibromatosis 2, Facial Nerve Diseases such as Facial Neuralgia, Melkersson-Rosenthal Syndrome, ocular motility disorders which includes amblyopia, nystagmus, oculomotor nerve paralysis, ophthalmoplegia such as Duane's Syndrome, Horner's Syndrome. Chronic Progressive External Ophthalmoplegia which includes Kearns Syndrome, Strabismus such as Esotropia and Exotropia, Oculomotor Nerve Paralysis, Optic Nerve Diseases such as Optic Atrophy which includes Hereditary Optic Atrophy, Optic Disk Drusen, Optic Neuritis such as Neuromyelitis Optica, Papilledema, Trigeminal Neuralgia, Vocal Cord Paralysis, Demyelinating Diseases such as Neuromyelitis Optica and Swayback, Diabetic neuropathies such as diabetic foot, nerve compression syndromes such as carpal tunnel syndrome, tarsal tunnel syndrome, thoracic outlet syndrome such as cervical rib syndrome, ulnar nerve compression syndrome, neuralgia such as causalgia, cervico-brachial neuralgia, facial neuralgia and trigeminal neuralgia, neuritis such as experimental allergic neuritis, optic neuritis, polyneuritis, polyradiculoneuritis and radiculities such as polyradiculitis, hereditary motor and sensory neuropathies such as Charcot-Marie Disease, Hereditary Optic Atrophy, Refsum's Disease, Hereditary Spastic Paraplegia and Werdnig-Hoffmann Disease, Hereditary Sensory and Autonomic Neuropathies which include Congenital Analgesia and Familial Dysautonomia, POEMS Syndrome, Sciatica. Gustatory Sweating and Tetany).

Infectious Disease

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by
5 initiating a new immune response. Alternatively, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

Viruses are one example of an infectious agent that can cause disease or
10 symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention. Examples of viruses, include, but are not limited to Examples of viruses, include, but are not limited to the following DNA and RNA viruses and viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Bimaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae,
15 Dengue, EBV, HIV, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza A, Influenza B, and parainfluenza), Papiloma virus, Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g.,
20 Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiollitis, respiratory syncytial virus, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), Japanese B encephalitis,
25 Junin, Chikungunya, Rift Valley fever, yellow fever, meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. polynucleotides or polypeptides, or agonists or antagonists of the invention,
30 can be used to treat or detect any of these symptoms or diseases. In specific

embodiments, polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat: meningitis, Dengue, EBV, and/or hepatitis (e.g., hepatitis B). In an additional specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat patients nonresponsive to one or more other commercially available hepatitis vaccines. In a further specific embodiment polynucleotides, polypeptides, or agonists or antagonists of the invention are used to treat AIDS.

Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, include, but not limited to, the following Gram-Negative and Gram-positive bacteria and bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Cryptococcus neoformans, Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia (e.g., Borrelia burgdorferi, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, E. coli (e.g., Enterotoxigenic E. coli and Enterohemorrhagic E. coli), Enterobacteriaceae (Klebsiella, Salmonella (e.g., Salmonella typhi, and Salmonella paratyphi), Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Mycobacterium leprae, Vibrio cholerae, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Meningococcal), Meissneria meningitidis, Pasteurellaceae Infections (e.g., Actinobacillus, Haemophilus (e.g., Haemophilus influenza type B), Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, Shigella spp., Staphylococcal, Meningiocoecal, Pneumococcal and Streptococcal (e.g., Streptococcus pneumoniae and Group B Streptococcus). These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning,

Typhoid, pneumonia, Gonorrhea, meningitis (e.g., meningitis types A and B), Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. Polynucleotides or polypeptides, agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases. In specific embodiments, Polynucleotides, polypeptides, agonists or antagonists of the invention are used to treat: tetanus, Diphtheria, botulism, and/or meningitis type B.

Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, the following families or class: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas and Sporozoans (e.g., Plasmodium virax, Plasmodium falciparum, Plasmodium malariae and Plasmodium ovale). These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), malaria, pregnancy complications, and toxoplasmosis. polynucleotides or polypeptides, or agonists or antagonists of the invention, can be used to treat or detect any of these symptoms or diseases.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

Regeneration

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of
5 tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs
10 (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vasculature (including vascular and lymphatics), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, polynucleotides or polypeptides, as well as agonists or antagonists
15 of the present invention, may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome,
20 and other tendon or ligament defects. A further example of tissue regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using
polynucleotides or polypeptides, as well as agonists or antagonists of the present
25 invention, to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or
30 other medical therapies), localized neuropathies, and central nervous system diseases

(e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotides or polypeptides, as well as agonists or antagonists of the present invention.

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Chemotaxis

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may have chemotaxis activity. A chemotactic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

Polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may increase chemotactic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotactic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that polynucleotides or polypeptides, as well as agonists or antagonists of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention could be used as an inhibitor of chemotaxis.

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Binding Activity

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit

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(antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

Additionally, the receptor to which the polypeptide of the present invention binds can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting (Coligan, et al., Current Protocols in Immun., 1(2), Chapter 5, (1991)). For example, expression cloning is employed
5 wherein polyadenylated RNA is prepared from a cell responsive to the polypeptides, for example, NIH3T3 cells which are known to contain multiple receptors for the FGF family proteins, and SC-3 cells, and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the polypeptides. Transfected cells which are grown on glass slides are
10 exposed to the polypeptide of the present invention, after they have been labelled. The polypeptides can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase.

Following fixation and incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and
15 re-transfected using an iterative sub-pooling and re-screening process, eventually yielding a single clones that encodes the putative receptor.

As an alternative approach for receptor identification, the labeled polypeptides can be photoaffinity linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE analysis and
20 exposed to X-ray film. The labeled complex containing the receptors of the polypeptides can be excised, resolved into peptide fragments, and subjected to protein microsequencing. The amino acid sequence obtained from microsequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the genes encoding the putative receptors.

Moreover, the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling") may be employed to modulate the activities of the polypeptide of the present invention thereby effectively generating agonists and antagonists of the polypeptide of the present invention. *See generally*, U.S. Patent Nos. 5,605,793, 5,811,238, 5,830,721,
25 5,834,252, and 5,837,458, and Patten, P. A., et al., *Curr. Opinion Biotechnol.* 8:724-
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33 (1997); Harayama, S. *Trends Biotechnol.* 16(2):76-82 (1998); Hansson, L. O., *et al.*, *J. Mol. Biol.* 287:265-76 (1999); and Lorenzo, M. M. and Blasco, R. *Biotechniques* 24(2):308-13 (1998) (each of these patents and publications are hereby incorporated by reference). In one embodiment, alteration of polynucleotides and corresponding polypeptides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments into a desired molecule by homologous, or site-specific, recombination. In another embodiment, polynucleotides and corresponding polypeptides may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of the polypeptide of the present invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules. In preferred embodiments, the heterologous molecules are family members. In further preferred embodiments, the heterologous molecule is a growth factor such as, for example, platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I), transforming growth factor (TGF)-alpha, epidermal growth factor (EGF), fibroblast growth factor (FGF), TGF-beta, bone morphogenetic protein (BMP)-2, BMP-4, BMP-5, BMP-6, BMP-7, activins A and B, decapentaplegic(dpp), 60A, OP-2, dorsalin, growth differentiation factors (GDFs), nodal, MIS, inhibin-alpha, TGF-beta1, TGF-beta2, TGF-beta3, TGF-beta5, and glial-derived neurotrophic factor (GDNF).

Other preferred fragments are biologically active fragments of the polypeptide of the present invention. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Additionally, this invention provides a method of screening compounds to identify those which modulate the action of the polypeptide of the present invention. An example of such an assay comprises combining a mammalian fibroblast cell, a polypeptide of the present invention, the compound to be screened and ^3H

thymidine under cell culture conditions where the fibroblast cell would normally proliferate. A control assay may be performed in the absence of the compound to be screened and compared to the amount of fibroblast proliferation in the presence of the compound to determine if the compound stimulates proliferation by determining the uptake of $^3\text{[H]}$ thymidine in each case. The amount of fibroblast cell proliferation is measured by liquid scintillation chromatography which measures the incorporation of $^3\text{[H]}$ thymidine. Both agonist and antagonist compounds may be identified by this procedure.

In another method, a mammalian cell or membrane preparation expressing a receptor for a polypeptide of the present invention is incubated with a labeled polypeptide of the present invention in the presence of the compound. The ability of the compound to enhance or block this interaction could then be measured. Alternatively, the response of a known second messenger system following interaction of a compound to be screened and the receptor is measured and the ability of the compound to bind to the receptor and elicit a second messenger response is measured to determine if the compound is a potential agonist or antagonist. Such second messenger systems include but are not limited to, cAMP guanylate cyclase, ion channels or phosphoinositide hydrolysis.

All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptides of the invention from suitably manipulated cells or tissues.

Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the present invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the present invention, (b) assaying a biological

activity, and (b) determining if a biological activity of the polypeptide has been altered.

Targeted Delivery

5 In another embodiment, the invention provides a method of delivering compositions to targeted cells expressing a receptor for a polypeptide of the invention, or cells expressing a cell bound form of a polypeptide of the invention.

As discussed herein, polypeptides or antibodies of the invention may be associated with heterologous polypeptides, heterologous nucleic acids, toxins, or
10 prodrugs via hydrophobic, hydrophilic, ionic and/or covalent interactions. In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (including antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic
15 protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

In another embodiment, the invention provides a method for the specific
20 destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention (e.g., polypeptides of the invention or antibodies of the invention) in association with toxins or cytotoxic prodrugs.

By "toxin" is meant compounds that bind and activate endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of
25 toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art. compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced
30 endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNase, alpha

toxin, ricin, abrin, *Pseudomonas* exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. By "cytotoxic prodrug" is meant a non-toxic compound that is converted by an enzyme, normally present in the cell, into a cytotoxic compound. Cytotoxic prodrugs that may be used according to the methods of the invention include, but are not limited to, glutamyl derivatives of benzoic acid mustard alkylating agent, phosphate derivatives of etoposide or mitomycin C, cytosine arabinoside, daunorubisin, and phenoxyacetamide derivatives of doxorubicin.

10 Drug Screening

Further contemplated is the use of the polypeptides of the present invention, or the polynucleotides encoding these polypeptides, to screen for molecules which modify the activities of the polypeptides of the present invention. Such a method would include contacting the polypeptide of the present invention with a selected compound(s) suspected of having antagonist or agonist activity, and assaying the activity of these polypeptides following binding.

This invention is particularly useful for screening therapeutic compounds by using the polypeptides of the present invention, or binding fragments thereof, in any of a variety of drug screening techniques. The polypeptide or fragment employed in such a test may be affixed to a solid support, expressed on a cell surface, free in solution, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. One may measure, for example, the formulation of complexes between the agent being tested and a polypeptide of the present invention.

Thus, the present invention provides methods of screening for drugs or any other agents which affect activities mediated by the polypeptides of the present invention. These methods comprise contacting such an agent with a polypeptide of the present invention or a fragment thereof and assaying for the presence of a

complex between the agent and the polypeptide or a fragment thereof, by methods well known in the art. In such a competitive binding assay, the agents to screen are typically labeled. Following incubation, free agent is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of a particular agent to bind to the polypeptides of the present invention.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to the polypeptides of the present invention, and is described in great detail in European Patent Application 84/03564, published on September 13, 1984, which is incorporated herein by reference herein. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with polypeptides of the present invention and washed. Bound polypeptides are then detected by methods well known in the art. Purified polypeptides are coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies may be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding polypeptides of the present invention specifically compete with a test compound for binding to the polypeptides or fragments thereof. In this manner, the antibodies are used to detect the presence of any peptide which shares one or more antigenic epitopes with a polypeptide of the invention.

Antisense And Ribozyme (Antagonists)

In specific embodiments, antagonists according to the present invention are nucleic acids corresponding to the sequences contained in SEQ ID NO:X, or the complementary strand thereof, and/or to nucleotide sequences contained in the cDNA contained in the related cDNA clone identified in Table 1. In one embodiment, antisense sequence is generated internally, by the organism, in another embodiment, the antisense sequence is separately administered (see, for example, O'Connor, J.,

Neurochem. 56:560 (1991). Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression. CRC Press, Boca Raton, FL (1988). Antisense technology can be used to control gene expression through antisense DNA or RNA, or through triple-helix formation. Antisense techniques are discussed for example, in Okano, J., Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, 5 CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance, Lee et al., Nucleic Acids Research 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1300 (1991). The methods are based on binding of a polynucleotide to a complementary DNA or RNA.

10 For example, the use of c-myc and c-myb antisense RNA constructs to inhibit the growth of the non-lymphocytic leukemia cell line HL-60 and other cell lines was previously described. (Wickstrom et al. (1988); Anfossi et al. (1989)). These experiments were performed in vitro by incubating cells with the oligoribonucleotide. A similar procedure for in vivo use is described in WO 91/15580. Briefly, a pair of 15 oligonucleotides for a given antisense RNA is produced as follows: A sequence complimentary to the first 15 bases of the open reading frame is flanked by an EcoRI site on the 5' end and a HindIII site on the 3' end. Next, the pair of oligonucleotides is heated at 90°C for one minute and then annealed in 2X ligation buffer (20mM TRIS HCl pH 7.5, 10mM MgCl₂, 10mM dithiothreitol (DTT) and 0.2 mM ATP) and 20 then ligated to the EcoRI/Hind III site of the retroviral vector PMV7 (WO 91/15580).

For example, the 5' coding portion of a polynucleotide that encodes the polypeptide of the present invention may be used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription 25 thereby preventing transcription and the production of the receptor. The antisense RNA oligonucleotide hybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into receptor polypeptide.

In one embodiment, the antisense nucleic acid of the invention is produced intracellularly by transcription from an exogenous sequence. For example, a vector or 30 a portion thereof, is transcribed, producing an antisense nucleic acid (RNA) of the

invention. Such a vector would contain a sequence encoding the antisense nucleic acid. Such a vector can remain episomal or become chromosomally integrated, as long as it can be transcribed to produce the desired antisense RNA. Such vectors can be constructed by recombinant DNA technology methods standard in the art. Vectors
5 can be plasmid, viral, or others known in the art, used for replication and expression in vertebrate cells. Expression of the sequence encoding the polypeptide of the present invention or fragments thereof, can be by any promoter known in the art to act in vertebrate, preferably human cells. Such promoters can be inducible or constitutive. Such promoters include, but are not limited to, the SV40 early promoter
10 region (Bernoist and Chambon, Nature 29:304-310 (1981), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto et al., Cell 22:787-797 (1980), the herpes thymidine promoter (Wagner et al., Proc. Natl. Acad. Sci. U.S.A. 78:1441-1445 (1981), the regulatory sequences of the metallothionein gene (Brinster, et al., Nature 296:39-42 (1982)), etc.

15 The antisense nucleic acids of the invention comprise a sequence complementary to at least a portion of an RNA transcript of a gene of the present invention. However, absolute complementarity, although preferred, is not required. A sequence "complementary to at least a portion of an RNA," referred to herein, means a sequence having sufficient complementarity to be able to hybridize with the
20 RNA, forming a stable duplex; in the case of double stranded antisense nucleic acids, a single strand of the duplex DNA may thus be tested, or triplex formation may be assayed. The ability to hybridize will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the larger the hybridizing nucleic acid, the more base mismatches with a RNA it may contain and still form a
25 stable duplex (or triplex as the case may be). One skilled in the art can ascertain a tolerable degree of mismatch by use of standard procedures to determine the melting point of the hybridized complex.

Oligonucleotides that are complementary to the 5' end of the message, e.g., the 5' untranslated sequence up to and including the AUG initiation codon, should work
30 most efficiently at inhibiting translation. However, sequences complementary to the

3' untranslated sequences of mRNAs have been shown to be effective at inhibiting translation of mRNAs as well. See generally, Wagner, R., 1994, *Nature* 372:333-335. Thus, oligonucleotides complementary to either the 5'- or 3'- non-translated, non-coding regions of polynucleotide sequences described herein could be used in an antisense approach to inhibit translation of endogenous mRNA. Oligonucleotides complementary to the 5' untranslated region of the mRNA should include the complement of the AUG start codon. Antisense oligonucleotides complementary to mRNA coding regions are less efficient inhibitors of translation but could be used in accordance with the invention. Whether designed to hybridize to the 5'-, 3'- or coding region of mRNA of the present invention, antisense nucleic acids should be at least six nucleotides in length, and are preferably oligonucleotides ranging from 6 to about 50 nucleotides in length. In specific aspects the oligonucleotide is at least 10 nucleotides, at least 17 nucleotides, at least 25 nucleotides or at least 50 nucleotides.

The polynucleotides of the invention can be DNA or RNA or chimeric mixtures or derivatives or modified versions thereof, single-stranded or double-stranded. The oligonucleotide can be modified at the base moiety, sugar moiety, or phosphate backbone, for example, to improve stability of the molecule, hybridization, etc. The oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al., 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre et al., 1987, *Proc. Natl. Acad. Sci.* 84:648-652; PCT Publication No. WO88/09810, published December 15, 1988) or the blood-brain barrier (see, e.g., PCT Publication No. WO89/10134, published April 25, 1988), hybridization-triggered cleavage agents. (See, e.g., Krol et al., 1988, *BioTechniques* 6:958-976) or intercalating agents. (See, e.g., Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide, hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

The antisense oligonucleotide may comprise at least one modified base moiety which is selected from the group including, but not limited to, 5-fluorouracil,

5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 5 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, 10 queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

The antisense oligonucleotide may also comprise at least one modified sugar moiety selected from the group including, but not limited to, arabinose, 15 2-fluoroarabinose, xylulose, and hexose.

In yet another embodiment, the antisense oligonucleotide comprises at least one modified phosphate backbone selected from the group including, but not limited to, a phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a 20 phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, and a formacetal or analog thereof.

In yet another embodiment, the antisense oligonucleotide is an a-anomeric oligonucleotide. An a-anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual b-units, the strands 25 run parallel to each other (Gautier et al., 1987, Nucl. Acids Res. 15:6625-6641). The oligonucleotide is a 2'-O-methylribonucleotide (Inoue et al., 1987, Nucl. Acids Res. 15:6131-6148), or a chimeric RNA-DNA analogue (Inoue et al., 1987, FEBS Lett. 215:327-330).

Polynucleotides of the invention may be synthesized by standard methods 30 known in the art, e.g. by use of an automated DNA synthesizer (such as are

commercially available from Biosearch, Applied Biosystems, etc.). As examples, phosphorothioate oligonucleotides may be synthesized by the method of Stein et al. (1988, Nucl. Acids Res. 16:3209), methylphosphonate oligonucleotides can be prepared by use of controlled pore glass polymer supports (Sarin et al., 1988, Proc. Natl. Acad. Sci. U.S.A. 85:7448-7451), etc.

While antisense nucleotides complementary to the coding region sequence could be used, those complementary to the transcribed untranslated region are most preferred.

Potential antagonists according to the invention also include catalytic RNA, or a ribozyme (See, e.g., PCT International Publication WO 90/11364, published October 4, 1990; Sarver et al, Science 247:1222-1225 (1990). While ribozymes that cleave mRNA at site specific recognition sequences can be used to destroy mRNAs, the use of hammerhead ribozymes is preferred. Hammerhead ribozymes cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The sole requirement is that the target mRNA have the following sequence of two bases: 5'-UG-3'. The construction and production of hammerhead ribozymes is well known in the art and is described more fully in Haseloff and Gerlach, Nature 334:585-591 (1988). There are numerous potential hammerhead ribozyme cleavage sites within the nucleotide sequence of SEQ ID NO:X. Preferably, the ribozyme is engineered so that the cleavage recognition site is located near the 5' end of the mRNA: i.e., to increase efficiency and minimize the intracellular accumulation of non-functional mRNA transcripts.

As in the antisense approach, the ribozymes of the invention can be composed of modified oligonucleotides (e.g. for improved stability, targeting, etc.) and should be delivered to cells which express in vivo. DNA constructs encoding the ribozyme may be introduced into the cell in the same manner as described above for the introduction of antisense encoding DNA. A preferred method of delivery involves using a DNA construct "encoding" the ribozyme under the control of a strong constitutive promoter, such as, for example, pol III or pol II promoter, so that transfected cells will produce sufficient quantities of the ribozyme to destroy

endogenous messages and inhibit translation. Since ribozymes unlike antisense molecules, are catalytic, a lower intracellular concentration is required for efficiency.

Antagonist/agonist compounds may be employed to inhibit the cell growth and proliferation effects of the polypeptides of the present invention on neoplastic
5 cells and tissues, i.e. stimulation of angiogenesis of tumors, and, therefore, retard or prevent abnormal cellular growth and proliferation, for example, in tumor formation or growth.

The antagonist/agonist may also be employed to prevent hyper-vascular diseases, and prevent the proliferation of epithelial lens cells after extracapsular
10 cataract surgery. Prevention of the mitogenic activity of the polypeptides of the present invention may also be desirable in cases such as restenosis after balloon angioplasty.

The antagonist/agonist may also be employed to prevent the growth of scar tissue during wound healing.

15 The antagonist/agonist may also be employed to treat the diseases described herein.

Thus, the invention provides a method of treating disorders or diseases, including but not limited to the disorders or diseases listed throughout this application, associated with overexpression of a polynucleotide of the present
20 invention by administering to a patient (a) an antisense molecule directed to the polynucleotide of the present invention, and/or (b) a ribozyme directed to the polynucleotide of the present invention.

Other Activities

25 A polypeptide, polynucleotide, agonist, or antagonist of the present invention, as a result of the ability to stimulate vascular endothelial cell growth, may be employed in treatment for stimulating re-vascularization of ischemic tissues due to various disease conditions such as thrombosis, arteriosclerosis, and other cardiovascular conditions. The polypeptide, polynucleotide, agonist, or antagonist of

the present invention may also be employed to stimulate angiogenesis and limb regeneration, as discussed above.

5 A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for treating wounds due to injuries, burns, post-operative tissue repair, and ulcers since they are mitogenic to various cells of different origins, such as fibroblast cells and skeletal muscle cells, and therefore, facilitate the repair or replacement of damaged or diseased tissue.

10 A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed stimulate neuronal growth and to treat and prevent neuronal damage which occurs in certain neuronal disorders or neuro-degenerative conditions such as Alzheimer's disease, Parkinson's disease, and AIDS-related complex. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may have the ability to stimulate chondrocyte growth, therefore, they may be employed to enhance bone and periodontal regeneration and aid in tissue transplants or bone
15 grafts.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be also be employed to prevent skin aging due to sunburn by stimulating keratinocyte growth.

20 A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for preventing hair loss, since FGF family members activate hair-forming cells and promotes melanocyte growth. Along the same lines, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be employed to stimulate growth and differentiation of hematopoietic cells and bone marrow cells when used in combination with other cytokines.

25 A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed to maintain organs before transplantation or for supporting cell culture of primary tissues. A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be employed for inducing tissue of mesodermal origin to differentiate in early embryos.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention
5 may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of
10 energy.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, cardiac rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or
15 Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide, polynucleotide, agonist, or antagonist of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals,
20 cofactors or other nutritional components.

The above-recited applications have uses in a wide variety of hosts. Such hosts include, but are not limited to, human, murine, rabbit, goat, guinea pig, camel, horse, mouse, rat, hamster, pig, micro-pig, chicken, goat, cow, sheep, dog, cat, non-human primate, and human. In specific embodiments, the host is a mouse, rabbit,
25 goat, guinea pig, chicken, rat, hamster, pig, sheep, dog or cat. In preferred embodiments, the host is a mammal. In most preferred embodiments, the host is a human.

Other Preferred Embodiments

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X in the range of positions identified as "Start" and "End" in columns 7 and 8 as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto, and/or the cDNA in

the related cDNA clone contained in the deposit. wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

5 Also preferred is a composition of matter comprising a DNA molecule which comprises a cDNA clone contained in the deposit.

 Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of the cDNA in the related cDNA clone
10 contained in the deposit.

 Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of an open reading frame sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

15 Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

 A further preferred embodiment is an isolated nucleic acid molecule
20 comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

 A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete
25 nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

 A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence
30 selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the

complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleotide sequence of SEQ ID NO:X; or the cDNA in the related cDNA clone identified in Table I which encodes a protein, wherein the method comprises a step of detecting in a biological sample

obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide
5 sequence of the cDNA in the related cDNA clone contained in the deposit.

Also preferred is the above method for diagnosing a pathological condition which comprises a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous
10 nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a
15 sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the related cDNA clone contained in the deposit. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is a composition of matter comprising isolated nucleic acid
20 molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a DNA microarray or "chip" of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, 50, 100, 150, 200, 250, 300, 500, 1000, 2000, 3000 or 4000 nucleotide sequences, wherein at least one sequence in said DNA microarray or "chip" is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected
25 from the group consisting of: a nucleotide sequence of SEQ ID NO:X or the complementary strand thereto; and a nucleotide sequence encoded by the cDNA in the cDNA clone referenced in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence
30 at least 90% identical to a sequence of at least about 10 contiguous amino acids in the

polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Also preferred is an isolated polypeptide comprising an amino acid sequence
5 at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid
10 sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid
15 sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and/or a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is an isolated polypeptide comprising an amino acid
20 sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino
acids is included in the amino acid sequence of a portion of said polypeptide encoded by the cDNA clone referenced in Table 1; a polypeptide encoded by SEQ ID NO:X;
25 and/or the polypeptide sequence of SEQ ID NO:Y.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table I.

5 Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of a polypeptide encoded by the cDNA clone referenced in Table I.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a
10 sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone contained in the deposit.

Further preferred is a method for detecting in a biological sample a
15 polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table I; which method comprises a step of comparing an amino acid
20 sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino
25 acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: a
30 polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X;

and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a nucleic acid sequence identified in Table 1 encoding a polypeptide, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence
5 selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said
10 polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1.

15 Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

20 Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a human protein comprising an amino acid sequence selected from
25 the group consisting of: polypeptide sequence of SEQ ID NO:Y; a polypeptide encoded by SEQ ID NO:X; and a polypeptide encoded by the cDNA in the related cDNA clone referenced in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an
30 increased level of a protein activity, which method comprises administering to such

an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to increase the level of said protein activity in said individual.

- 5 Also preferred is a method of treatment of an individual in need of a decreased level of a protein activity, which method comprised administering to such an individual a Therapeutic comprising an amount of an isolated polypeptide, polynucleotide, immunogenic fragment or analogue thereof, binding agent, antibody, or antigen binding fragment of the claimed invention effective to decrease the level of
- 10 said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

*Examples**Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample*

5 Each deposited cDNA clone is contained in a plasmid vector. Table 5 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The following correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 5 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

	<u>Vector Used to Construct Library</u>	<u>Corresponding Deposited Plasmid</u>
	Lambda Zap	pBluescript (pBS)
	Uni-Zap XR	pBluescript (pBS)
15	Zap Express	pBK
	lafmid BA	plafmid BA
	pSport1	pSport1
	pCMVSport 2.0	pCMVSport 2.0
	pCMVSport 3.0	pCMVSport 3.0
20	pCR [®] 2.1	pCR [®] 2.1

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS. The S and K refers to the orientation of the polylinker to the T7 and T3

primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the fl origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the fl ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 5, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited by reference to Table 2 and 5 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone referenced in Table 1.

TABLE 5

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HUKA HUKB HUKC HUKD HUKF HUKG	Human Uterine Cancer	Lambda ZAP II	LP01
HCNA HCNB	Human Colon	Lambda Zap II	LP01
HFFA	Human Fetal Brain, random primed	Lambda Zap II	LP01
HTWA	Resting T-Cell	Lambda ZAP II	LP01
HBQA	Early Stage Human Brain, random primed	Lambda ZAP II	LP01
HLMB HLMF HLMG HLMH HLMI HLMJ HLMM HLMN	breast lymph node CDNA library	Lambda ZAP II	LP01
HCOA HCQB	human colon cancer	Lambda ZAP II	LP01
HMEA HMEC HMEF HMEI HMEJ HMEK HMEI	Human Microvascular Endothelial Cells, fract. A	Lambda ZAP II	LP01
HUSA HUSC	Human Umbilical Vein Endothelial Cells, fract. A	Lambda ZAP II	LP01
HLQA HLOB	Hepatocellular Tumor	Lambda ZAP II	LP01
HHGA HHGB HHGC HHGD	Hemangiopericytoma	Lambda ZAP II	LP01
HSDM	Human Striatum Depression, re-rescue	Lambda ZAP II	LP01
HUSH	H Umbilical Vein Endothelial Cells, frac A, re-excision	Lambda ZAP II	LP01
HSGS	Salivary gland, subtracted	Lambda ZAP II	LP01
HFXA HFXB HFXC HFXD HFXE HFXF HFXG HFXH	Brain frontal cortex	Lambda ZAP II	LP01
HPQA HPQB HPQC	PERM TF274	Lambda ZAP II	LP01
HFXJ HFXK	Brain Frontal Cortex, re-excision	Lambda ZAP II	LP01
HCWA HCWB HCWC HCWD HCWE HCWF HCWG HCWH HCWI HCWJ HCWK	CD34 positive cells (Cord Blood)	ZAP Express	LP02
HCUA HCUB HCUC	CD34 depleted Buffy Coat (Cord Blood)	ZAP Express	LP02
HRSM	A-14 cell line	ZAP Express	LP02
HRSA	A1-CELL LINE	ZAP Express	LP02
HCUD HCUE HCUF HCUG HCUH HCUJ	CD34 depleted Buffy Coat (Cord Blood), re-excision	ZAP Express	LP02
HBXE HBXF HBXG	H. Whole Brain #2, re-excision	ZAP Express	LP02
HRLM	L8 cell line	ZAP Express	LP02
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP02
HUDA HUDB HUDC	Testes	ZAP Express	LP02
HHTM HHTN HHTO	H. hypothalamus, frac A:re-excision	ZAP Express	LP02
HHTL	H. hypothalamus, frac A	ZAP Express	LP02
HASA HASD	Human Adult Spleen	Uni-ZAP XR	LP03
HFKC HFKD HFKE HFKF HFKG	Human Fetal Kidney	Uni-ZAP XR	LP03
HE8A HE8B HE8C HE8D HE8E HE8F HE8M HE8N	Human 8 Week Whole Embryo	Uni-ZAP XR	LP03
HGBA HGBD HGBE HGBF HGBG HGBH HGBI	Human Gall Bladder	Uni-ZAP XR	LP03
HLHA HLHB HLHC HLHD HLHE	Human Fetal Lung III	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HLHF HLHG HLHH HLHQ			
HPMA HPMB HPMC HPMD HPME HPMF HPMG HPMH	Human Placenta	Uni-ZAP XR	LP03
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP03
HSIA HSIC HSID HSIE	Human Adult Small Intestine	Uni-ZAP XR	LP03
HTEA HTEB HTEC HTED HTEE HTEF HTEG HTEH HTEI HTEJ HTEK	Human Testes	Uni-ZAP XR	LP03
HTPA HTPB HTPC HTPD HTPF	Human Pancreas Tumor	Uni-ZAP XR	LP03
HTTA HTTB HTTC HTTD HTTE HTTF	Human Testes Tumor	Uni-ZAP XR	LP03
HAPA HAPB HAPC HAPM	Human Adult Pulmonary	Uni-ZAP XR	LP03
HETA HETB HETC HETD HETE HETF HETG HETH HETI	Human Endometrial Tumor	Uni-ZAP XR	LP03
HHFB HHFC HHFD HHFE HHFF HHFG HHFH HHFI	Human Fetal Heart	Uni-ZAP XR	LP03
HHPB HHPD HHPF HHPG HHPH	Human Hippocampus	Uni-ZAP XR	LP03
HCE1 HCE2 HCE3 HCE4 HCE5 HCEB HCEC HCED HCEE HCEF HCEG	Human Cerebellum	Uni-ZAP XR	LP03
HUVB HUV C HUVD HUVE	Human Umbilical Vein. Endo. remake	Uni-ZAP XR	LP03
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP03
HTAA HTAB HTAC HTAD HTAE	Human Activated T-Cells	Uni-ZAP XR	LP03
HFEA HFEB HFEC	Human Fetal Epithelium (Skin)	Uni-ZAP XR	LP03
HJPA HJPB HJPC HJPD	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Uni-ZAP XR	LP03
HESA	Human epithelioid sarcoma	Uni-Zap XR	LP03
HLTA HLTB HLTC HLTD HLTE HLTF	Human T-Cell Lymphoma	Uni-ZAP XR	LP03
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP03
HRDA HRDB HRDC HRDD HRDE HRDF	Human Rhabdomyosarcoma	Uni-ZAP XR	LP03
HCAA HCAB HCAC	Cem cells cyclohexamide treated	Uni-ZAP XR	LP03
HRGA HRGB HRGC HRGD	Raji Cells. cyclohexamide treated	Uni-ZAP XR	LP03
HSUA HSUB HSUC HSUM	Supt Cells. cyclohexamide treated	Uni-ZAP XR	LP03
HT4A HT4C HT4D	Activated T-Cells. 12 hrs.	Uni-ZAP XR	LP03
HE9A HE9B HE9C HE9D HE9E HE9F HE9G HE9H HE9M HE9N	Nine Week Old Early Stage Human	Uni-ZAP XR	LP03
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP03
HT5A	Activated T-Cells. 24 hrs.	Uni-ZAP XR	LP03
HFGA HFGM	Human Fetal Brain	Uni-ZAP XR	LP03
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP03
HBGB HBGD	Human Primary Breast Cancer	Uni-ZAP XR	LP03
HBNA HBNB	Human Normal Breast	Uni-ZAP XR	LP03
HCAS	Cem Cells. cyclohexamide treated. subtra	Uni-ZAP XR	LP03
HHPS	Human Hippocampus. subtracted	pBS	LP03
HKCS HKCU	Human Colon Cancer. subtracted	pBS	LP03
HRGS	Raji cells. cyclohexamide treated. subtracted	pBS	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HSUT	Supt cells. cyclohexamide treated. differentially expressed	pBS	LP03
HT4S	Activated T-Cells. 12 hrs. subtracted	Uni-ZAP XR	LP03
HCDA HCDB HCDC HCDD HCDE	Human Chondrosarcoma	Uni-ZAP XR	LP03
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP03
HTLA HTLB HTLC HTLD HTLE HTLF	Human adult testis. large inserts	Uni-ZAP XR	LP03
HLMA HLMB HLMD	Breast Lymph node cDNA library	Uni-ZAP XR	LP03
H6EA H6EB H6EC	HL-60. PMA 4H	Uni-ZAP XR	LP03
HTXA HTXB HTXC HTXD HTXE HTXF HTXG HTXH	Activated T-Cell (12hs)/Thiouridine labelledEco	Uni-ZAP XR	LP03
HNFA HNFB HNFC HNFD HNFE HNFF HNFG HNFI HNFI	Human Neutrophil. Activated	Uni-ZAP XR	LP03
HTOB HTOC	HUMAN TONSILS. FRACTION 2	Uni-ZAP XR	LP03
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP03
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP03
HORB	Human OB HOS treated (10 nM E2) fraction I	Uni-ZAP XR	LP03
HSVA HSVB HSVC	Human Chronic Synovitis	Uni-ZAP XR	LP03
HROA	HUMAN STOMACH	Uni-ZAP XR	LP03
HBJA HBJB HBJC HBJD HBJE HBJF HBJG HBJH HBJI HBJJ HBJK	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP03
HCRA HCRB HCRC	human corpus colosum	Uni-ZAP XR	LP03
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP03
HDSA	Dermatofibrosarcoma Protuberance	Uni-ZAP XR	LP03
HMWA HMWB HMWC HMWD HMWE HMWF HMWG HMWH HMWI HMWJ	Bone Marrow Cell Line (RS4;11)	Uni-ZAP XR	LP03
HSOA	stomach cancer (human)	Uni-ZAP XR	LP03
HERA	SKIN	Uni-ZAP XR	LP03
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP03
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP03
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP03
HBCA HBCB	H. Lymph node breast Cancer	Uni-ZAP XR	LP03
HPWT	Human Prostate BPH. re-excision	Uni-ZAP XR	LP03
HFVG HFVH HFVI	Fetal Liver. subtraction II	pBS	LP03
HNFI	Human Neutrophils. Activated. re-excision	pBS	LP03
HBMB HBMC HBMD	Human Bone Marrow. re-excision	pBS	LP03
HKML HKMM HKMN	H. Kidney Medulla. re-excision	pBS	LP03
HKIX HKIY	H. Kidney Cortex. subtracted	pBS	LP03
HADT	H. Amygdala Depression. subtracted	pBS	LP03
H6AS	HL-60. untreated. subtracted	Uni-ZAP XR	LP03
H6ES	HL-60. PMA 4H. subtracted	Uni-ZAP XR	LP03
H6BS	HL-60. RA 4h. Subtracted	Uni-ZAP XR	LP03
H6CS	HL-60. PMA 1d. subtracted	Uni-ZAP XR	LP03
HTXJ HTXK	Activated T-cell(12h)/Thiouridine-re-	Uni-ZAP XR	LP03

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
	excision		
HMSA HMSB HMSC HMSE HMSF HMSG HMSH HMSI HMSJ HMSK	Monocyte activated	Uni-ZAP XR	LP03
HAGA HAGB HAGC HAGD HAGE HAGF	Human Amygdala	Uni-ZAP XR	LP03
HSRA HSRB HSRE	STROMAL -OSTEOCLASTOMA	Uni-ZAP XR	LP03
HSRD HSRF HSRG HSRH	Human Osteoclastoma Stromal Cells - unamplified	Uni-ZAP XR	LP03
HSQA HSQB HSQC HSQD HSQE HSQF HSQG	Stromal cell TF274	Uni-ZAP XR	LP03
HSKA HSKB HSKC HSKD HSKE HSKF HSKZ	Smooth muscle, serum treated	Uni-ZAP XR	LP03
HSLA HSLB HSLC HSLD HSE HSEF HSLG	Smooth muscle control	Uni-ZAP XR	LP03
HSDA HSDD HSDE HSDF HSDG HSDH	Spinal cord	Uni-ZAP XR	LP03
HPWS	Prostate-BPH subtracted II	pBS	LP03
HSKW HSKX HSKY	Smooth Muscle- HASTE normalized	pBS	LP03
HFPB HFPC HFPD	H. Frontal cortex.epileptic:re-excision	Uni-ZAP XR	LP03
HSDI HSDJ HSDK	Spinal Cord. re-excision	Uni-ZAP XR	LP03
HSKN HSKO	Smooth Muscle Serum Treated. Norm	pBS	LP03
HSKG HSKH HSKI	Smooth muscle, serum induced.re-exc	pBS	LP03
HFCB HFCB HFCC HFCD HFCE HFCF	Human Fetal Brain	Uni-ZAP XR	LP04
HPTA HPTB HPTD	Human Pituitary	Uni-ZAP XR	LP04
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP04
HE6B HE6C HE6D HE6E HE6F HE6G HE6S	Human Whole Six Week Old Embryo	Uni-ZAP XR	LP04
HSSA HSSB HSSC HSSD HSSE HSSF HSSG HSSH HSSI HSSJ HSSK	Human Synovial Sarcoma	Uni-ZAP XR	LP04
HE7T	7 Week Old Early Stage Human, subtracted	Uni-ZAP XR	LP04
HEPA HEPB HEPD	Human Epididymus	Uni-ZAP XR	LP04
HSNA HSNB HSNC HSNM HSNM	Human Synovium	Uni-ZAP XR	LP04
HPFB HPFC HPFD HPFE	Human Prostate Cancer. Stage C fraction	Uni-ZAP XR	LP04
HE2A HE2D HE2E HE2H HE2I HE2M HE2N HE2O	12 Week Old Early Stage Human	Uni-ZAP XR	LP04
HE2B HE2C HE2F HE2G HE2P HE2Q	12 Week Old Early Stage Human. II	Uni-ZAP XR	LP04
HPTS HPTT HPTU	Human Pituitary. subtracted	Uni-ZAP XR	LP04
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP04
HAQA HAQB HAQC HAOD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP04
HWTB HWTB HWTB	wilm's tumor	Uni-ZAP XR	LP04
HBSD	Bone Cancer. re-excision	Uni-ZAP XR	LP04
HSGB	Salivary gland. re-excision	Uni-ZAP XR	LP04
HSJA HSJB HSJC	Smooth muscle-ILb induced	Uni-ZAP XR	LP04
HSXA HSXB HSXC HSXD	Human Substantia Nigra	Uni-ZAP XR	LP04
HSJA HSHB HSHC	Smooth muscle. IL1b induced	Uni-ZAP XR	LP04
HOUA HOUB HOUC HOUD HOUE	Adipocytes	Uni-ZAP XR	LP04

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP04
HELA HELB HELC HELD HELE HELF HELG HELH	Endothelial cells-control	Uni-ZAP XR	LP04
HEMA HEMB HEMC HEMD HEME HEMF HEMG HEMH	Endothelial-induced	Uni-ZAP XR	LP04
HBIA HBIB HBIC	Human Brain. Striatum	Uni-ZAP XR	LP04
HHSA HHSB HHSC HHSD HHSE	Human Hypothalamus.Schizophrenia	Uni-ZAP XR	LP04
HNGA HNGB HNGC HNGD HNGE HNGF HNGG HNGH HNGI HNGJ	neutrophils control	Uni-ZAP XR	LP04
HNHA HNHB HNHC HNHD HNHE HNHF HNHG HNHH HNHI HNHI	Neutrophils IL-1 and LPS induced	Uni-ZAP XR	LP04
HSDB HSDC	STRIATUM DEPRESSION	Uni-ZAP XR	LP04
HHPT	Hypothalamus	Uni-ZAP XR	LP04
HSAT HSAU HSAV HSAW HSAX HSAY HSAZ	Anergic T-cell	Uni-ZAP XR	LP04
HBMS HBMT HBMU HBMV HBMW HBMX	Bone marrow	Uni-ZAP XR	LP04
HOEA HOEB HOEC HOED HOEE HOEF HOEJ	Osteoblasts	Uni-ZAP XR	LP04
HAIA HAIB HAIC HAID HAIE HAIF	Epithelial-TNF α and INF induced	Uni-ZAP XR	LP04
HTGA HTGB HTGC HTGD	Apoptotic T-cell	Uni-ZAP XR	LP04
HMCA HMCB HMCC HMCD HMCE	Macrophage-oxLDL	Uni-ZAP XR	LP04
HMAA HMAB HMCA HMAD HMAE HMAF HMAG	Macrophage (GM-CSF treated)	Uni-ZAP XR	LP04
HPHA	Normal Prostate	Uni-ZAP XR	LP04
HPIA HPIB HPIC	LNCAP prostate cell line	Uni-ZAP XR	LP04
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP04
HOSE HOSF HOSG	Human Osteoclastoma. re-excision	Uni-ZAP XR	LP04
HTGE HTGF	Apoptotic T-cell. re-excision	Uni-ZAP XR	LP04
HMAJ HMAK	H Macrophage (GM-CSF treated), re-excision	Uni-ZAP XR	LP04
HACB HACC HACD	Human Adipose Tissue. re-excision	Uni-ZAP XR	LP04
HPPA	H. Frontal Cortex. Epileptic	Uni-ZAP XR	LP04
HFAA HFAB HFAC HFAD HFAE	Alzheimers. spongy change	Uni-ZAP XR	LP04
HFAM	Frontal Lobe, Dementia	Uni-ZAP XR	LP04
HMIA HMIB HMIC	Human Manic Depression Tissue	Uni-ZAP XR	LP04
HTSA HTSE HTSF HTSG HTSH	Human Thymus	pBS	LP05
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBS	LP05
HSAA HSAB HSAC	HSA 172 Cells	pBS	LP05
HSBA HSBB HSBC HSBM	HSC172 cells	pBS	LP05
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBS	LP05
HJBA HJBB HJBC HJBD	Jurkat T-Cell. S phase	pBS	LP05
HAFA HAFB	Aorta endothelial cells + TNF- α	pBS	LP05
HAWA HAWB HAWC	Human White Adipose	pBS	LP05
HTNA HTNB	Human Thyroid	pBS	LP05
HONA	Normal Ovary. Premenopausal	pBS	LP05
HARA HARB	Human Adult Retina	pBS	LP05

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HLJA HLJB	Human Lung	pCMVSPORT 1	LP06
HOFM HOFN HOFO	H. Ovarian Tumor. II. OV5232	pCMVSPORT 2.0	LP07
HOGA HOGB HOGC	OV 10-3-95	pCMVSPORT 2.0	LP07
HCGL	CD34+cells. II	pCMVSPORT 2.0	LP07
HDLA	Hodgkin's Lymphoma I	pCMVSPORT 2.0	LP07
HDTA HDTB HDTC HDTD HDTE	Hodgkin's Lymphoma II	pCMVSPORT 2.0	LP07
HKAA HKAB HKAC HKAD HKAE HKAF HKAG HKAH	Keratinocyte	pCMVSPORT2.0	LP07
HCIM	CAPFINDER. Crohn's Disease. lib 2	pCMVSPORT 2.0	LP07
HKAL	Keratinocyte. lib 2	pCMVSPORT2.0	LP07
HKAT	Keratinocyte. lib 3	pCMVSPORT2.0	LP07
HNDA	Nasal polyps	pCMVSPORT2.0	LP07
HDRA	H. Primary Dendritic Cells.lib 3	pCMVSPORT2.0	LP07
HOHA HOHB HOHC	Human Osteoblasts II	pCMVSPORT2.0	LP07
HLDA HLDB HLDC	Liver. Hepatoma	pCMVSPORT3.0	LP08
HLDN HLDO HLDP	Human Liver. normal	pCMVSPORT3.0	LP08
HMTA	pBMC stimulated w/ poly I/C	pCMVSPORT3.0	LP08
HNTA	NTERA2. control	pCMVSPORT3.0	LP08
HDP A HDPB HDPC HDPD HDPF HDPG HDPH HDPI HDPJ HDPK	Primary Dendritic Cells. lib 1	pCMVSPORT3.0	LP08
HDPM HDPN HDPO HDPP	Primary Dendritic cells.frac 2	pCMVSPORT3.0	LP08
HMUA HMUB HMUC	Myeloid Progenitor Cell Line	pCMVSPORT3.0	LP08
HHEA HHEB HHEC HHED	T Cell helper I	pCMVSPORT3.0	LP08
HHEM HHEN HHEO HHEP	T cell helper II	pCMVSPORT3.0	LP08
HEQA HEQB HEQC	Human endometrial stromal cells	pCMVSPORT3.0	LP08
HJMA HJMB	Human endometrial stromal cells-treated with progesterone	pCMVSPORT3.0	LP08
HSWA HSWB HSWC	Human endometrial stromal cells-treated with estradiol	pCMVSPORT3.0	LP08
HSYA HSYB HSYC	Human Thymus Stromal Cells	pCMVSPORT3.0	LP08
HLWA HLWB HLWC	Human Placenta	pCMVSPORT3.0	LP08
HRAA HRAB HRAC	Rejected Kidney. lib 4	pCMVSPORT3.0	LP08
HMTM	PCR. pBMC I/C treated	PCR II	LP09
HMJA	H. Meningioma. M6	pSport 1	LP10
HMKA HMKB HMKC HMKD HMKE	H. Meningioma. M1	pSport 1	LP10
HUSG HUSI	Human umbilical vein endothelial cells. IL-4 induced	pSport 1	LP10
HUSX HUSY	Human Umbilical Vein Endothelial Cells. uninduced	pSport 1	LP10
HOFA	Ovarian Tumor I. OV5232	pSport 1	LP10
HCFA HCFB HCFC HCFC	T-Cell PHA 16 hrs	pSport 1	LP10
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport 1	LP10
HADA HADC HADD HADE HADF HADG	Human Adipose	pSport 1	LP10
HOVA HOVB HOVC	Human Ovary	pSport 1	LP10
HTWB HTWC HTWD HTWE HTWF	Resting T-Cell Library.II	pSport 1	LP10

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HMMA	Spleen metastatic melanoma	pSport 1	LP10
HLYA HLYB HLYC HLYD HLYE	Spleen. Chronic lymphocytic leukemia	pSport 1	LP10
HCGA	CD34+ cell. 1	pSport 1	LP10
HEOM HEON	Human Eosinophils	pSport 1	LP10
HTDA	Human Tonsil. Lib 3	pSport 1	LP10
HSPA	Salivary Gland. Lib 2	pSport 1	LP10
HCHA HCHB HCHC	Breast Cancer cell line. MDA 36	pSport 1	LP10
HCHM HCHN	Breast Cancer Cell line. angiogenic	pSport 1	LP10
HCIA	Crohn's Disease	pSport 1	LP10
HDAA HDAB HDAC	HEL cell line	pSport 1	LP10
HABA	Human Astrocyte	pSport 1	LP10
HUFA HUFB HUFC	Ulcerative Colitis	pSport 1	LP10
HNTM	NTERA2 + retinoic acid. 14 days	pSport 1	LP10
HDQA	Primary Dendritic cells.CapFinder2. frac 1	pSport 1	LP10
HDQM	Primary Dendritic Cells. CapFinder. frac 2	pSport 1	LP10
HLDX	Human Liver. normal.CapFinder	pSport 1	LP10
HULA HULB HULC	Human Dermal Endothelial Cells.untreated	pSport1	LP10
HUMA	Human Dermal Endothelial cells.treated	pSport1	LP10
HCJA	Human Stromal Endometrial fibroblasts, untreated	pSport1	LP10
HCJM	Human Stromal endometrial fibroblasts, treated w/ estradiol	pSport1	LP10
HEDA	Human Stromal endometrial fibroblasts, treated with progesterone	pSport1	LP10
HFNA	Human ovary tumor cell OV350721	pSport1	LP10
HKGA HKGB HKGC HKGD	Merkel Cells	pSport1	LP10
HISA HISB HISC	Pancreas Islet Cell Tumor	pSport1	LP10
HLSA	Skin. burned	pSport 1	LP10
HBZA	Prostate.BPH. Lib 2	pSport 1	LP10
HBZS	Prostate BPH.Lib 2. subtracted	pSport 1	LP10
HFIA HFIB HFIC	Synovial Fibroblasts (control)	pSport 1	LP10
HFIH HFII HFII	Synovial hypoxia	pSport 1	LP10
HFIT HFIU HFIV	Synovial IL-1/TNF stimulated	pSport 1	LP10
HGCA	Mesangial cell. frac 1	pSport1	LP10
HMVA HMVB HMVC	Bone Marrow Stromal Cell. untreated	pSport1	LP10
HFIX HFII HFIZ	Synovial Fibroblasts (IL1/TNF). subt	pSport1	LP10
HFOX HFOY HFOZ	Synovial hypoxia-RSF subtracted	pSport 1	LP10
HMQA HMOB HMQC HMQD	Human Activated Monocytes	Uni-ZAP XR	LP11
HLIA HLIB HLIC	Human Liver	pCMVSPORT 1	LP012
HHBA HHBB HHBC HHBD HHBE	Human Heart	pCMVSPORT 1	LP012
HBBA HBBB	Human Brain	pCMVSPORT 1	LP012
HLJA HLJB HLJC HLJD HLJE	Human Lung	pCMVSPORT 1	LP012
HOGA HOGB HOGC	Ovarian Tumor	pCMVSPORT 2.0	LP012

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HTJM	Human Tonsils. Lib 2	pCMVSPORT 2.0	LP012
HAMF HAMG	KMH2	pCMVSPORT 3.0	LP012
HABA HAJB HAJC	L428	pCMVSPORT 3.0	LP012
HWBA HWBB HWBC HWBD HWBE	Dendritic cells. pooled	pCMVSPORT 3.0	LP012
HWAA HWAB HWAC HWAD HWAE	Human Bone Marrow. treated	pCMVSPORT 3.0	LP012
HYAA HYAB HYAC	B Cell lymphoma	pCMVSPORT 3.0	LP012
HWHG HWHH HWHI	Healing groin wound. 6.5 hours post incision	pCMVSPORT 3.0	LP012
HWHP HWHQ HWHR	Healing groin wound: 7.5 hours post incision	pCMVSPORT 3.0	LP012
HARM	Healing groin wound - zero hr post-incision (control)	pCMVSPORT 3.0	LP012
HBIM	Olfactory epithelium: nasalcavity	pCMVSPORT 3.0	LP012
HWDA	Healing Abdomen wound: 70&90 min post incision	pCMVSPORT 3.0	LP012
HWEA	Healing Abdomen Wound:15 days post incision	pCMVSPORT 3.0	LP012
HWJA	Healing Abdomen Wound:21&29 days	pCMVSPORT 3.0	LP012
HNAL	Human Tongue. Lib 2	pSport I	LP012
HMJA	H. Meningioma. M6	pSport I	LP012
HMK A HMK B HMK C HMK D HMK E	H. Meningioma. M1	pSport I	LP012
HOFA	Ovarian Tumor I. OV5232	pSport I	LP012
HCFA HCFB HCFC HCFC	T-Cell PHA 16 hrs	pSport I	LP012
HCFL HCFM HCFN HCFO	T-Cell PHA 24 hrs	pSport I	LP012
HMM A HMM B HMM C	Spleen metastatic melanoma	pSport I	LP012
HTDA	Human Tonsil. Lib 3	pSport I	LP012
HDBA	Human Fetal Thymus	pSport I	LP012
HDDA	Pericardium	pSport I	LP012
HBZA	Prostate.BPH. Lib 2	pSport I	LP012
HWCA	Larynx tumor	pSport I	LP012
HWKA	Normal lung	pSport I	LP012
HSMB	Bone marrow stroma.treated	pSport I	LP012
HBHM	Normal trachea	pSport I	LP012
HLFC	Human Larynx	pSport I	LP012
HLLB	Siebbin Polyposis	pSport I	LP012
HNIA	Mammary Gland	pSport I	LP012
HNJB	Palate carcinoma	pSport I	LP012
HNKA	Palate normal	pSport I	LP012
HMZA	Pharynx carcinoma	pSport I	LP012
HABG	Cheek Carcinoma	pSport I	LP012
HMZM	Pharynx Carcinoma	pSport I	LP012
HDRM	Larynx Carcinoma	pSport I	LP012
HVAA	Pancreas normal PCA4 No	pSport I	LP012
HICA	Tongue carcinoma	pSport I	LP012
HUKA HUKB HUKC HUKD HUK E	Human Uterine Cancer	Lambda ZAP II	LP013
HFFA	Human Fetal Brain. random primed	Lambda ZAP II	LP013
HTUA	Activated T-cell labeled with 4-thioluri	Lambda ZAP II	LP013
HBQA	Early Stage Human Brain. random primed	Lambda ZAP II	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HMEB	Human microvascular Endothelial cells, fract. B	Lambda ZAP II	LP013
HUSH	Human Umbilical Vein Endothelial cells, fract. A, re-excision	Lambda ZAP II	LP013
HLQC HLQD	Hepatocellular tumor, re-excision	Lambda ZAP II	LP013
HTWJ HTWK HTWL	Resting T-cell, re-excision	Lambda ZAP II	LP013
HF6S	Human Whole 6 week Old Embryo (II), subt	pBluescript	LP013
HHPS	Human Hippocampus, subtracted	pBluescript	LP013
HLIS	LNCAP, differential expression	pBluescript	LP013
HLHS HLHT	Early Stage Human Lung, Subtracted	pBluescript	LP013
HSUS	Supt cells, cyclohexamide treated, subtracted	pBluescript	LP013
HSUT	Supt cells, cyclohexamide treated, differentially expressed	pBluescript	LP013
HSDS	H. Striatum Depression, subtracted	pBluescript	LP013
HPTZ	Human Pituitary, Subtracted VII	pBluescript	LP013
HSDX	H. Striatum Depression, subt II	pBluescript	LP013
HSDZ	H. Striatum Depression, subt	pBluescript	LP013
HPBA HPBB HPBC HPBD HPBE	Human Pineal Gland	pBluescript SK-	LP013
HRTA	Colorectal Tumor	pBluescript SK-	LP013
HSBA HSBB HSBC HSBM	HSC172 cells	pBluescript SK-	LP013
HJAA HJAB HJAC HJAD	Jurkat T-cell G1 phase	pBluescript SK-	LP013
HJBA HJBB HJBC HJBD	Jurkat T-cell, S1 phase	pBluescript SK-	LP013
HTNA HTNB	Human Thyroid	pBluescript SK-	LP013
HAHA HAHB	Human Adult Heart	Uni-ZAP XR	LP013
HE6A	Whole 6 week Old Embryo	Uni-ZAP XR	LP013
HFCA HFCB HFCC HFCD HFCE	Human Fetal Brain	Uni-ZAP XR	LP013
HFKE HFKE HFKE HFKE HFKE	Human Fetal Kidney	Uni-ZAP XR	LP013
HGBA HGBD HGBE HGBF HGBG	Human Gall Bladder	Uni-ZAP XR	LP013
HPRA HPRB HPRC HPRD	Human Prostate	Uni-ZAP XR	LP013
HTEA HTEB HTEC HTED HTEE	Human Testes	Uni-ZAP XR	LP013
HTTA HTTB HTTC HTTD HTTE	Human Testes Tumor	Uni-ZAP XR	LP013
HYBA HYBB	Human Fetal Bone	Uni-ZAP XR	LP013
HFLA	Human Fetal Liver	Uni-ZAP XR	LP013
HHFB HHFC HHFD HHFE HHFF	Human Fetal Heart	Uni-ZAP XR	LP013
HUVB HUV C HUVD HUVE	Human Umbilical Vein, End. remake	Uni-ZAP XR	LP013
HTHB HTHC HTHD	Human Thymus	Uni-ZAP XR	LP013
HSTA HSTB HSTC HSTD	Human Skin Tumor	Uni-ZAP XR	LP013
HTAA HTAB HTAC HTAD HTAE	Human Activated T-cells	Uni-ZAP XR	LP013
HFEA HFEB HFEC	Human Fetal Epithelium (skin)	Uni-ZAP XR	LP013
HJPA HJPB HJPC HJPD	Human Jurkat Membrane Bound Polysomes	Uni-ZAP XR	LP013
HESA	Human Epithelioid Sarcoma	Uni-ZAP XR	LP013
HALS	Human Adult Liver, Subtracted	Uni-ZAP XR	LP013
HFTA HFTB HFTC HFTD	Human Fetal Dura Mater	Uni-ZAP XR	LP013
HCAA HCAB HCAC	Cem cells, cyclohexamide treated	Uni-ZAP XR	LP013
HRGA HRGB HRGC HRGD	Raji Cells, cyclohexamide treated	Uni-ZAP XR	LP013
HE9A HE9B HE9C HE9D HE9E	Nine Week Old Early Stage Human	Uni-ZAP XR	LP013

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HSFA	Human Fibrosarcoma	Uni-ZAP XR	LP013
HATA HATB HATC HATD HATE	Human Adrenal Gland Tumor	Uni-ZAP XR	LP013
HTRA	Human Trachea Tumor	Uni-ZAP XR	LP013
HE2A HE2D HE2E HE2H HE2I	12 Week Old Early Stage Human	Uni-ZAP XR	LP013
HE2B HE2C HE2F HE2G HE2P	12 Week Old Early Stage Human. II	Uni-ZAP XR	LP013
HNEA HNEB HNEC HNED HNEE	Human Neutrophil	Uni-ZAP XR	LP013
HBGA	Human Primary Breast Cancer	Uni-ZAP XR	LP013
HPTS HPTT HPTU	Human Pituitary, subtracted	Uni-ZAP XR	LP013
HMQA HMQB HMQC HMOD	Human Activated Monocytes	Uni-ZAP XR	LP013
HOAA HOAB HOAC	Human Osteosarcoma	Uni-ZAP XR	LP013
HTOA HTOD HTOE HTOF HTOG	human tonsils	Uni-ZAP XR	LP013
HMGB	Human OB MG63 control fraction I	Uni-ZAP XR	LP013
HOPB	Human OB HOS control fraction I	Uni-ZAP XR	LP013
HOQB	Human OB HOS treated (1 nM E2) fraction I	Uni-ZAP XR	LP013
HAUA HAUB HAUC	Amniotic Cells - TNF induced	Uni-ZAP XR	LP013
HAQA HAQB HAQC HAOD	Amniotic Cells - Primary Culture	Uni-ZAP XR	LP013
HROA HROC	HUMAN STOMACH	Uni-ZAP XR	LP013
HBJA HBJB HBJC HBJD HBJE	HUMAN B CELL LYMPHOMA	Uni-ZAP XR	LP013
HODA HODB HODC HODD	human ovarian cancer	Uni-ZAP XR	LP013
HCPA	Corpus Callosum	Uni-ZAP XR	LP013
HSOA	stomach cancer (human)	Uni-ZAP XR	LP013
HERA	SKIN	Uni-ZAP XR	LP013
HMDA	Brain-medulloblastoma	Uni-ZAP XR	LP013
HGLA HGLB HGLD	Glioblastoma	Uni-ZAP XR	LP013
HWTA HWTB HWTG	wilm's tumor	Uni-ZAP XR	LP013
HEAA	H. Atrophic Endometrium	Uni-ZAP XR	LP013
HAPN HAPO HAPB HAPQ HAPR	Human Adult Pulmonary:re-excision	Uni-ZAP XR	LP013
HLTG HLTH	Human T-cell lymphoma:re-excision	Uni-ZAP XR	LP013
HAHC HAHD HAHE	Human Adult Heart:re-excision	Uni-ZAP XR	LP013
HAGA HAGB HAGC HAGD HAGE	Human Amygdala	Uni-ZAP XR	LP013
HSJA HSJB HSJC	Smooth muscle-IL1b induced	Uni-ZAP XR	LP013
HSJA HSJB HSJC	Smooth muscle. IL1b induced	Uni-ZAP XR	LP013
HPWA HPWB HPWC HPWD HPWE	Prostate BPH	Uni-ZAP XR	LP013
HPJA HPJB HPJC	LNCAP prostate cell line	Uni-ZAP XR	LP013
HPJA HPJB HPJC	PC3 Prostate cell line	Uni-ZAP XR	LP013
HBTA	Bone Marrow Siroma. TNF&LPS ind	Uni-ZAP XR	LP013
HMCF HMCB HMCH HMCJ HMCJ	Macrophage-oxLDL: re-excision	Uni-ZAP XR	LP013
HAGG HAGH HAGI	Human Amygdala:re-excision	Uni-ZAP XR	LP013
HACA	H. Adipose Tissue	Uni-ZAP XR	LP013
HKFB	K562 + PMA (36 hrs):re-excision	ZAP Express	LP013
HCWT HCWU HCWV	CD34 positive cells (cord blood):re-ex	ZAP Express	LP013
HBWA	Whole brain	ZAP Express	LP013
HBXA HBXB HBXC HBXD	Human Whole Brain #2 - Oligo dT > 1.5Kb	ZAP Express	LP013
HAVM	Temporal cortex-Alzheimer	pT-Adv	LP014
HAVT	Hippocampus. Alzheimer Subtracted	pT-Adv	LP014

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HHAS	CHME Cell Line	Uni-ZAP XR	LP014
HAJR	Larynx normal	pSport 1	LP014
HWLE HWLF HWLG HWLH	Colon Normal	pSport 1	LP014
HCRM HCRN HCRO	Colon Carcinoma	pSport 1	LP014
HWLI HWLJ HWLK	Colon Normal	pSport 1	LP014
HWLQ HWLR HWLS HWLT	Colon Tumor	pSport 1	LP014
HBFM	Gastrocnemius Muscle	pSport 1	LP014
HBOD HBOE	Quadriceps Muscle	pSport 1	LP014
HBKD HBKE	Soleus Muscle	pSport 1	LP014
HCCM	Pancreatic Langerhans	pSport 1	LP014
HWGA	Larynx carcinoma	pSport 1	LP014
HWGM HWGN	Larynx carcinoma	pSport 1	LP014
HWLA HWLB HWLC	Normal colon	pSport 1	LP014
HWLM HWLN	Colon Tumor	pSport 1	LP014
HVAM HVAN HVAO	Pancreas Tumor	pSport 1	LP014
HWGQ	Larynx carcinoma	pSport 1	LP014
HAQM HAQN	Salivary Gland	pSport 1	LP014
HASM	Stomach: normal	pSport 1	LP014
HBCM	Uterus: normal	pSport 1	LP014
HCDM	Testis: normal	pSport 1	LP014
HDJM	Brain: normal	pSport 1	LP014
HEFM	Adrenal Gland: normal	pSport 1	LP014
HBAA	Rectum normal	pSport 1	LP014
HFDN	Rectum tumour	pSport 1	LP014
HGAM	Colon: normal	pSport 1	LP014
HHMM	Colon: tumour	pSport 1	LP014
HCLB HCLC	Human Lung Cancer	Lambda Zap II	LP015
HRLA	L1 Cell line	ZAP Express	LP015
HHAM	Hypothalamus, Alzheimer's	pCMV Sport 3.0	LP015
HKBA	Ku 812F Basophils Line	pSport 1	LP015
HS2S	Saos2, Dexamethasone Treated	pSport 1	LP016
HASA	Lung Carcinoma A549 TNFalpha activated	pSport 1	LP016
HTFM	TF-1 Cell Line GM-CSF Treated	pSport 1	LP016
HYAS	Thyroid Tumour	pSport 1	LP016
HUTS	Larynx Normal	pSport 1	LP016
HXOA	Larynx Tumor	pSport 1	LP016
HEAH	Ea.hy.926 cell line	pSport 1	LP016
HINA	Adenocarcinoma Human	pSport 1	LP016
HRMA	Lung Mesothelium	pSport 1	LP016
HLCL	Human Pre-Differentiated Adipocytes	Uni-Zap XR	LP017
HS2A	Saos2 Cells	pSport 1	LP020
HS2I	Saos2 Cells: Vitamin D3 Treated	pSport 1	LP020
HUCM	CHME Cell Line, untreated	pSport 1	LP020
HEPN	Aryepiglottis Normal	pSport 1	LP020
HPSN	Sinus Piniformis Tumour	pSport 1	LP020
HNSA	Stomach Normal	pSport 1	LP020

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HNSM	Stomach Tumour	pSport 1	LP020
HNLA	Liver Normal Met5No	pSport 1	LP020
HUTA	Liver Tumour Met 5 Tu	pSport 1	LP020
HOCN	Colon Normal	pSport 1	LP020
HOCT	Colon Tumor	pSport 1	LP020
HTNT	Tongue Tumour	pSport 1	LP020
HLXN	Larynx Normal	pSport 1	LP020
HLXT	Larynx Tumour	pSport 1	LP020
HTYN	Thymus	pSport 1	LP020
HPLN	Placenta	pSport 1	LP020
HTNG	Tongue Normal	pSport 1	LP020
HZAA	Thyroid Normal (SDCA2 No)	pSport 1	LP020
HWES	Thyroid Thyroiditis	pSport 1	LP020
HFHD	Ficolled Human Stromal Cells. 5Fu treated	pTrip1Ex2	LP021
HFHM.HFHN	Ficolled Human Stromal Cells. Untreated	pTrip1Ex2	LP021
HPCI	Hep G2 Cells. lambda library	lambda Zap-CMV XR	LP021
HBCA.HBCB.HBCC	H. Lymph node breast Cancer	Uni-ZAP XR	LP021
HCOK	Chondrocytes	pSPORT1	LP022
HDCA. HDCB. HDCC	Dendritic Cells From CD34 Cells	pSPORT1	LP022
HDMA. HDMB	CD40 activated monocyte dendritic cells	pSPORT1	LP022
HDDM. HDDN. HDDO	LPS activated derived dendritic cells	pSPORT1	LP022
HPCR	Hep G2 Cells. PCR library	lambda Zap-CMV XR	LP022
HAAA. HAAB. HAAC	Lung. Cancer (4005313A3): Invasive Poorly Differentiated Lung Adenocarcinoma	pSPORT1	LP022
HIPA. HIPB. HIPC	Lung. Cancer (4005163 B7): Invasive. Poorly Diff. Adenocarcinoma. Metastatic	pSPORT1	LP022
HOOH. HOOI	Ovary. Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm. Low Malignant Pot	pSPORT1	LP022
HIDA	Lung. Normal: (4005313 B1)	pSPORT1	LP022
HUJA.HUJB.HUJC.HUJD.HUJE	B-Cells	pCMVSport 3.0	LP022
HNOA.HNOB.HNOC.HNOD	Ovary. Normal: (9805C040R)	pSPORT1	LP022
HNLM	Lung. Normal: (4005313 B1)	pSPORT1	LP022
HSCL	Stromal Cells	pSPORT1	LP022
HAAX	Lung. Cancer: (4005313 A3) Invasive Poorly-differentiated Metastatic lung adenocarcinoma	pSPORT1	LP022
HUUA.HUUB.HUUC.HUUD	B-cells (unstimulated)	pTrip1Ex2	LP022
HWWA.HWWB.HWWC.HWWD.HWWE.HWWF.HWWG	B-cells (stimulated)	pSPORT1	LP022
HCCC	Colon. Cancer: (9808C064R)	pCMVSport 3.0	LP023
HPDO HPDP HPDQ HPDR HPD	Ovary. Cancer (9809C332): Poorly differentiated adenocarcinoma	pSport 1	LP023
HPCO HPCP HPCQ HPCT	Ovary. Cancer (15395A1F): Grade II Papillary Carcinoma	pSport 1	LP023
HOCM HOCO HOCQ HOCQ	Ovary. Cancer: (15799A1F) Poorly differentiated carcinoma	pSport 1	LP023

Libraries owned by Catalog	Catalog Description	Vector	ATCC Deposit
HCBM HCBN HCBO	Breast. Cancer: (4004943 A5)	pSport 1	LP023
HNBT HNBU HNBV	Breast. Normal: (4005522B2)	pSport 1	LP023
HBCP HBCO	Breast. Cancer: (4005522 A2)	pSport 1	LP023
HBCJ	Breast. Cancer: (9806C012R)	pSport 1	LP023
HSAM HSAN	Stromal cells 3.88	pSport 1	LP023
HVCA HVCB HVCC HVCD	Ovary. Cancer: (4004332 A2)	pSport 1	LP023
HSCK HSEN HSEO	Stromal cells (HBM3.18)	pSport 1	LP023
HSCP HSCQ	stromal cell clone 2.5	pSport 1	LP023
HUXA	Breast Cancer: (4005385 A2)	pSport 1	LP023
HCOM HCON HCOO HCOP HCOQ	Ovary. Cancer (4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	pSport 1	LP023
HBNM	Breast. Cancer: (9802C020E)	pSport 1	LP023
HVVA HVVB HVVC HVVD HVVE	Human Bone Marrow, treated	pSport 1	LP023

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 5. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to the nucleotide sequence of SEQ ID NO:X.

- 5 Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ^{32}P - γ -ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, Cold Spring, NY (1982).)
- 10 The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate.
- 15 These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

- Alternatively, two primers of 17-20 nucleotides derived from both ends of the
- 20 nucleotide sequence of SEQ ID NO:X are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 μl of reaction mixture with 0.5 μg of the above cDNA template. A convenient reaction mixture is 1.5-5 mM MgCl_2 , 0.01% (w/v) gelatin, 20 μM each of dATP, dCTP, dGTP, dTTP, 25
- 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be
- 30 the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., Nucleic Acids Res. 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the sequence corresponding to SEQ ID NO:X, according to the method described in Example 1. (See also, Sambrook.)

Example 3: Tissue specific expression analysis

The Human Genome Sciences, Inc. (HGS) database is derived from sequencing tissue specific cDNA libraries. Libraries generated from a particular tissue are selected and the specific tissue expression pattern of EST groups or assembled contigs within these libraries is determined by comparison of the expression patterns of those groups or contigs within the entire database. ESTs which show tissue specific expression are selected.

The original clone from which the specific EST sequence was generated, is obtained from the catalogued library of clones and the insert amplified by PCR using methods known in the art. The PCR product is denatured then transferred in 96 well format to a nylon membrane (Schleicher and Scheull) generating an array filter of tissue specific clones. Housekeeping genes, maize genes, and known tissue specific genes are included on the filters. These targets can be used in signal normalization and to validate assay sensitivity. Additional targets are included to monitor probe length and specificity of hybridization.

Radioactively labeled hybridization probes are generated by first strand cDNA synthesis per the manufacturer's instructions (Life Technologies) from mRNA/RNA samples prepared from the specific tissue being analyzed. The hybridization probes are purified by gel exclusion chromatography, quantitated, and hybridized with the array filters in hybridization bottles at 65°C overnight. The filters are washed under stringent conditions and signals are captured using a Fuji phosphorimager.

Data is extracted using AIS software and following background subtraction, signal normalization is performed. This includes a normalization of filter-wide

expression levels between different experimental runs. Genes that are differentially expressed in the tissue of interest are identified and the full length sequence of these clones is generated.

5

Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This
10 primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is
15 analyzed on either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

20

Example 5: Bacterial Expression of a Polypeptide

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as
25 BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a

ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the *E. coli* strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.⁶⁰⁰) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate. pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear
5 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM imidazole. Imidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at
10 4° C or frozen at -80° C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains:
15 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

20 DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or
25 Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

Example 6: Purification of a Polypeptide from an Inclusion Body

The following alternative method can be used to purify a polypeptide expressed in *E. coli* when it is present in the form of inclusion bodies. Unless
5 otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate
10 amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfluidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate
15 is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the
20 pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA
25 by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The
30 filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive

Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

5 Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40
10 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A_{280} monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

15 The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 μ g of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL
20 assays.

Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System

25 In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40")

is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak *Drosophila* promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., *Virology* 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon, is amplified using the PCR protocol described in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("GeneClean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue

(Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

Five μ g of a plasmid containing the polynucleotide is co-transfected with 1.0 μ g of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One μ g of BaculoGold™ virus DNA and 5 μ g of the plasmid are mixed in a sterile well of a microtiter plate containing 50 μ l of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 μ l Lipofectin plus 90 μ l Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 μ l of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the
5 medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 μ Ci of 35 S-methionine and 5 μ Ci 35 S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by
10 SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

15 *Example 8: Expression of a Polypeptide in Mammalian Cells*

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals
20 required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLV1, HIV1 and the early promoter of the
25 cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC

67109), pCMVSPORT 2.0. and pCMVSPORT 3.0. Mammalian host cells that could be used include human HeLa, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

5 Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as DHFR, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

10 The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker
15 is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the
20 production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No. 209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the
25 CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

30 Specifically, the plasmid pC6, for example, is digested with appropriate

restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If a naturally occurring signal sequence is used to produce the polypeptide of the present invention, the vector does not need a second signal peptide. Alternatively, if a naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five μ g of the expression plasmid pC6 or pC4 is cotransfected with 0.5 μ g of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 μ M, 2 μ M, 5 μ M, 10 mM, 20 mM).

The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200 μ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

5 *Example 9: Protein Fusions*

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5: see
10 also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the half-life time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can
15 increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an
20 IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

25 For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note
30 that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will

not be produced.

If the naturally occurring signal sequence is used to produce the polypeptide of the present invention, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to
5 include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

```
GGGATCCGGAGCCCAAATCTTCTGACAAACTCACACATGCCCACCGTGC
CCAGCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCAAAA
10 CCCAAGGACACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGT
GGTGGACGTAAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGG
ACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTA
CAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACT
GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCA
15 ACCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAAC
CACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAG
GTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGT
GGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCT
CCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTG
20 GACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCA
TGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG
GTAAATGAGTGCGACGGCCGCGACTCTAGAGGAT (SEQ ID NO:919)
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Example 10: Production of an Antibody from a Polypeptide

25

a) Hybridoma Technology

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) As one example of such methods, cells expressing polypeptide of the present invention are administered to an animal to
30 induce the production of sera containing polyclonal antibodies. In a preferred method,

a preparation of polypeptide of the present invention is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

5 Monoclonal antibodies specific for polypeptide of the present invention are prepared using hybridoma technology. (Kohler et al., *Nature* 256:495 (1975); Kohler et al., *Eur. J. Immunol.* 6:511 (1976); Kohler et al., *Eur. J. Immunol.* 6:292 (1976); Hammerling et al., in: *Monoclonal Antibodies and T-Cell Hybridomas*, Elsevier, N.Y., pp. 563-681 (1981)). In general, an animal (preferably a mouse) is immunized
10 with polypeptide of the present invention or, more preferably, with a secreted polypeptide of the present invention-expressing cell. Such polypeptide-expressing cells are cultured in any suitable tissue culture medium, preferably in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000
15 U/ml of penicillin, and about 100 µg/ml of streptomycin.

 The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are
20 selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (*Gastroenterology* 80:225-232 (1981)). The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide of the present invention.

 Alternatively, additional antibodies capable of binding to polypeptide of the
25 present invention can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then
30 used to produce hybridoma cells, and the hybridoma cells are screened to identify

clones which produce an antibody whose ability to bind to the polypeptide of the present invention-specific antibody can be blocked by polypeptide of the present invention. Such antibodies comprise anti-idiotypic antibodies to the polypeptide of the present invention-specific antibody and are used to immunize an animal to induce
5 formation of further polypeptide of the present invention-specific antibodies.

For in vivo use of antibodies in humans, an antibody is "humanized". Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric and humanized antibodies are known in the art and are discussed herein.
10 (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

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b) Isolation Of Antibody Fragments Directed Against Polypeptide of the Present Invention From A Library Of scFvs

Naturally occurring V-genes isolated from human PBLs are constructed into a library of antibody fragments which contain reactivities against polypeptide of the present invention to which the donor may or may not have been exposed (see e.g.,
20 U.S. Patent 5,885,793 incorporated herein by reference in its entirety).

Rescue of the Library. A library of scFvs is constructed from the RNA of human PBLs as described in PCT publication WO 92/01047. To rescue phage displaying antibody fragments, approximately 10⁹ E. coli harboring the phagemid are used to inoculate 50 ml of 2xTY containing 1% glucose and 100 µg/ml of ampicillin
25 (2xTY-AMP-GLU) and grown to an O.D. of 0.8 with shaking. Five ml of this culture is used to inoculate 50 ml of 2xTY-AMP-GLU. 2 x 10⁸ TU of delta gene 3 helper (M13 delta gene III, see PCT publication WO 92/01047) are added and the culture incubated at 37°C for 45 minutes without shaking and then at 37°C for 45 minutes
30 with shaking. The culture is centrifuged at 4000 r.p.m. for 10 min. and the pellet

resuspended in 2 liters of 2xTY containing 100 µg/ml ampicillin and 50 ug/ml kanamycin and grown overnight. Phage are prepared as described in PCT publication WO 92/01047.

M13 delta gene III is prepared as follows: M13 delta gene III helper phage
5 does not encode gene III protein, hence the phage(mid) displaying antibody fragments have a greater avidity of binding to antigen. Infectious M13 delta gene III particles are made by growing the helper phage in cells harboring a pUC19 derivative supplying the wild type gene III protein during phage morphogenesis. The culture is incubated for 1 hour at 37° C without shaking and then for a further hour at 37°C with
10 shaking. Cells are spun down (IEC-Centra 8,400 r.p.m. for 10 min), resuspended in 300 ml 2xTY broth containing 100 µg ampicillin/ml and 25 µg kanamycin/ml (2xTY-AMP-KAN) and grown overnight, shaking at 37°C. Phage particles are purified and concentrated from the culture medium by two PEG-precipitations (Sambrook et al., 1990), resuspended in 2 ml PBS and passed through a 0.45 µm filter (Minisart NML;
15 Sartorius) to give a final concentration of approximately 10¹³ transducing units/ml (ampicillin-resistant clones).

Panning of the Library. Immunotubes (Nunc) are coated overnight in PBS with 4 ml of either 100 µg/ml or 10 µg/ml of a polypeptide of the present invention. Tubes are blocked with 2% Marvel-PBS for 2 hours at 37°C and then washed 3 times
20 in PBS. Approximately 10¹³ TU of phage is applied to the tube and incubated for 30 minutes at room temperature tumbling on an over and under turntable and then left to stand for another 1.5 hours. Tubes are washed 10 times with PBS 0.1% Tween-20 and 10 times with PBS. Phage are eluted by adding 1 ml of 100 mM triethylamine and rotating 15 minutes on an under and over turntable after which the solution is
25 immediately neutralized with 0.5 ml of 1.0M Tris-HCl, pH 7.4. Phage are then used to infect 10 ml of mid-log E. coli TG1 by incubating eluted phage with bacteria for 30 minutes at 37°C. The E. coli are then plated on TYE plates containing 1% glucose and 100 µg/ml ampicillin. The resulting bacterial library is then rescued with delta gene 3 helper phage as described above to prepare phage for a subsequent round of
30 selection. This process is then repeated for a total of 4 rounds of affinity purification

with tube-washing increased to 20 times with PBS. 0.1% Tween-20 and 20 times with PBS for rounds 3 and 4.

Characterization of Binders. Eluted phage from the 3rd and 4th rounds of selection are used to infect E. coli HB 2151 and soluble scFv is produced (Marks, et al., 1991) from single colonies for assay. ELISAs are performed with microtitre plates coated with either 10 pg/ml of the polypeptide of the present invention in 50 mM bicarbonate pH 9.6. Clones positive in ELISA are further characterized by PCR fingerprinting (see, e.g., PCT publication WO 92/01047) and then by sequencing. These ELISA positive clones may also be further characterized by techniques known in the art, such as, for example, epitope mapping, binding affinity, receptor signal transduction, ability to block or competitively inhibit antibody/antigen binding, and competitive agonistic or antagonistic activity.

Example 11: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X; and/or the nucleotide sequence of the related cDNA in the cDNA clone contained in a deposited library. Suggested PCR conditions consist of 35 cycles at 95 degrees C for 30 seconds; 60-120 seconds at 52-58 degrees C; and 60-120 seconds at 70 degrees C, using buffer solutions described in Sidransky et al., Science 252:706 (1991).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre

Technologies). The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

- 5 PCR products is cloned into T-tailed vectors as described in Holton et al., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

- 10 Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-triphosphate (Boehringer Mannheim), and FISH performed as described in Johnson et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the
- 15 corresponding genomic locus.

- Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera
- 20 (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and
- 25 translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 12: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 13: Formulation

The invention also provides methods of treatment and/or prevention of

diseases or disorders (such as, for example, any one or more of the diseases or disorders disclosed herein) by administration to a subject of an effective amount of a Therapeutic. By therapeutic is meant a polynucleotides or polypeptides of the invention (including fragments and variants), agonists or antagonists thereof, and/or
5 antibodies thereto, in combination with a pharmaceutically acceptable carrier type (e.g., a sterile carrier).

The Therapeutic will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the Therapeutic alone), the site of
10 delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of the Therapeutic administered parenterally per dose will be in the range of about
15 1 ug/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the Therapeutic is typically administered at a
20 dose rate of about 1 ug/kg/hour to about 50 ug/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Therapeutics can be are administered orally, rectally, parenterally,
25 intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any. The term "parenteral" as used herein refers to modes of administration which include
30 intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and

intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics are administered orally, rectally, parenterally, intracisternally, intravaginally, 5 intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, 10 intrasternal, subcutaneous and intraarticular injection and infusion.

Therapeutics of the invention are also suitably administered by sustained-release systems. Suitable examples of sustained-release Therapeutics include suitable polymeric materials (such as, for example, semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules), suitable hydrophobic materials 15 (for example as an emulsion in an acceptable oil) or ion exchange resins, and sparingly soluble derivatives (such as, for example, a sparingly soluble salt).

Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman et al., Biopolymers 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (Langer et al., 20 J. Biomed. Mater. Res. 15:167-277 (1981), and Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (Langer et al., Id.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988).

Sustained-release Therapeutics also include liposomally entrapped Therapeutics of the invention (see generally, Langer, *Science* 249:1527-1533 (1990); 25 Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 317 -327 and 353-365 (1989)). Liposomes containing the Therapeutic are prepared by methods known per se: DE 3,218,121; Epstein et al., Proc. Natl. Acad. Sci. (USA) 82:3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci.(USA) 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 30 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos.

4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal Therapeutic.

5 In yet an additional embodiment, the Therapeutics of the invention are delivered by way of a pump (*see* Langer, *supra*; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987); Buchwald et al., Surgery 88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)).

Other controlled release systems are discussed in the review by Langer
10 (*Science* 249:1527-1533 (1990)).

For parenteral administration, in one embodiment, the Therapeutic is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and
15 concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to the Therapeutic.

Generally, the formulations are prepared by contacting the Therapeutic uniformly and intimately with liquid carriers or finely divided solid carriers or both.
20 Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

25 The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten
30 residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum

albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar
5 alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The Therapeutic is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or
10 stabilizers will result in the formation of polypeptide salts.

Any pharmaceutical used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutics generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a
15 stopper pierceable by a hypodermic injection needle.

Therapeutics ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous Therapeutic solution,
20 and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized Therapeutic using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the Therapeutics of the invention. Associated with such container(s) can be a notice in the form prescribed by
25 a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the Therapeutics may be employed in conjunction with other therapeutic compounds.

The Therapeutics of the invention may be administered alone or in
30 combination with adjuvants. Adjuvants that may be administered with the

Therapeutics of the invention include, but are not limited to, alum, alum plus deoxycholate (ImmunoAg), MTP-PE (Biocine Corp.), QS21 (Genentech, Inc.), BCG, and MPL. In a specific embodiment, Therapeutics of the invention are administered in combination with alum. In another specific embodiment, Therapeutics of the invention are administered in combination with QS-21. Further adjuvants that may be administered with the Therapeutics of the invention include, but are not limited to, Monophosphoryl lipid immunomodulator, AdjuVax 100a, QS-21, QS-18, CRL1005, Aluminum salts, MF-59, and Virosomal adjuvant technology. Vaccines that may be administered with the Therapeutics of the invention include, but are not limited to, vaccines directed toward protection against MMR (measles, mumps, rubella), polio, varicella, tetanus/diphtheria, hepatitis A, hepatitis B, haemophilus influenzae B, whooping cough, pneumonia, influenza, Lyme's Disease, rotavirus, cholera, yellow fever, Japanese encephalitis, poliomyelitis, rabies, typhoid fever, and pertussis. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through separate intravenous lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

The Therapeutics of the invention may be administered alone or in combination with other therapeutic agents. Therapeutic agents that may be administered in combination with the Therapeutics of the invention, include but not limited to, other members of the TNF family, chemotherapeutic agents, antibiotics, steroidal and non-steroidal anti-inflammatories, conventional immunotherapeutic agents, cytokines and/or growth factors. Combinations may be administered either concomitantly, e.g., as an admixture, separately but simultaneously or concurrently; or sequentially. This includes presentations in which the combined agents are administered together as a therapeutic mixture, and also procedures in which the combined agents are administered separately but simultaneously, e.g., as through

separate intravenous lines into the same individual. Administration "in combination" further includes the separate administration of one of the compounds or agents given first, followed by the second.

In one embodiment, the Therapeutics of the invention are administered in combination with members of the TNF family. TNF, TNF-related or TNF-like molecules that may be administered with the Therapeutics of the invention include, but are not limited to, soluble forms of TNF-alpha, lymphotoxin-alpha (LT-alpha, also known as TNF-beta), LT-beta (found in complex heterotrimer LT-alpha2-beta), OPGL, FasL, CD27L, CD30L, CD40L, 4-1BBL, DcR3, OX40L, TNF-gamma (International Publication No. WO 96/14328), AIM-1 (International Publication No. WO 97/33899), endokine-alpha (International Publication No. WO 98/07880), TR6 (International Publication No. WO 98/30694), OPG, and neutrokine-alpha (International Publication No. WO 98/18921, OX40, and nerve growth factor (NGF), and soluble forms of Fas, CD30, CD27, CD40 and 4-1BB, TR2 (International Publication No. WO 96/34095), DR3 (International Publication No. WO 97/33904), DR4 (International Publication No. WO 98/32856), TR5 (International Publication No. WO 98/30693), TR6 (International Publication No. WO 98/30694), TR7 (International Publication No. WO 98/41629), TRANK, TR9 (International Publication No. WO 98/56892), TR10 (International Publication No. WO 98/54202), 312C2 (International Publication No. WO 98/06842), and TR12, and soluble forms CD154, CD70, and CD153.

In certain embodiments, Therapeutics of the invention are administered in combination with antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors. Nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, RETROVIR™ (zidovudine/AZT), VIDEX™ (didanosine/ddI), HIVID™ (zalcitabine/ddC), ZERIT™ (stavudine/d4T), EPIVIR™ (lamivudine/3TC), and COMBIVIR™ (zidovudine/lamivudine). Non-nucleoside reverse transcriptase inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are

not limited to, VIRAMUNE™ (nevirapine), RESCRIPTOR™ (delavirdine), and SUSTIVA™ (efavirenz). Protease inhibitors that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, CRIXIVAN™ (indinavir), NORVIR™ (ritonavir), INVIRASE™ (saquinavir), and VIRACEPT™ (nelfinavir). In a specific embodiment, antiretroviral agents, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and/or protease inhibitors may be used in any combination with Therapeutics of the invention to treat AIDS and/or to prevent or treat HIV infection.

In other embodiments, Therapeutics of the invention may be administered in combination with anti-opportunistic infection agents. Anti-opportunistic agents that may be administered in combination with the Therapeutics of the invention, include, but are not limited to, TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, ATOVAQUONE™, ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, ETHAMBUTOL™, RIFABUTIN™, CLARITHROMYCIN™, AZITHROMYCIN™, GANCICLOVIR™, FOSCARNET™, CIDOFOVIR™, FLUCONAZOLE™, ITRACONAZOLE™, KETOCONAZOLE™, ACYCLOVIR™, FAMCICOLVIR™, PYRIMETHAMINE™, LEUCOVORIN™, NEUPOGEN™ (filgrastim/G-CSF), and LEUKINE™ (sargramostim/GM-CSF). In a specific embodiment, Therapeutics of the invention are used in any combination with TRIMETHOPRIM-SULFAMETHOXAZOLE™, DAPSONE™, PENTAMIDINE™, and/or ATOVAQUONE™ to prophylactically treat or prevent an opportunistic *Pneumocystis carinii* pneumonia infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ISONIAZID™, RIFAMPIN™, PYRAZINAMIDE™, and/or ETHAMBUTOL™ to prophylactically treat or prevent an opportunistic *Mycobacterium avium* complex infection. In another specific embodiment, Therapeutics of the invention are used in any combination with RIFABUTIN™, CLARITHROMYCIN™, and/or AZITHROMYCIN™ to prophylactically treat or prevent an opportunistic *Mycobacterium tuberculosis* infection. In another specific embodiment, Therapeutics

of the invention are used in any combination with GANCICLOVIR™, FOSCARNET™, and/or CIDOFOVIR™ to prophylactically treat or prevent an opportunistic cytomegalovirus infection. In another specific embodiment, Therapeutics of the invention are used in any combination with FLUCONAZOLE™, ITRACONAZOLE™, and/or KETOCONAZOLE™ to prophylactically treat or prevent an opportunistic fungal infection. In another specific embodiment, Therapeutics of the invention are used in any combination with ACYCLOVIR™ and/or FAMCICOLVIR™ to prophylactically treat or prevent an opportunistic herpes simplex virus type I and/or type II infection. In another specific embodiment, Therapeutics of the invention are used in any combination with PYRIMETHAMINE™ and/or LEUCOVORIN™ to prophylactically treat or prevent an opportunistic *Toxoplasma gondii* infection. In another specific embodiment, Therapeutics of the invention are used in any combination with LEUCOVORIN™ and/or NEUPOGEN™ to prophylactically treat or prevent an opportunistic bacterial infection.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antiviral agent. Antiviral agents that may be administered with the Therapeutics of the invention include, but are not limited to, acyclovir, ribavirin, amantadine, and remantidine.

In a further embodiment, the Therapeutics of the invention are administered in combination with an antibiotic agent. Antibiotic agents that may be administered with the Therapeutics of the invention include, but are not limited to, amoxicillin, beta-lactamases, aminoglycosides, beta-lactam (glycopeptide), beta-lactamases, Clindamycin, chloramphenicol, cephalosporins, ciprofloxacin, ciprofloxacin, erythromycin, fluoroquinolones, macrolides, metronidazole, penicillins, quinolones, rifampin, streptomycin, sulfonamide, tetracyclines, trimethoprim, trimethoprim-sulfamthoxazole, and vancomycin.

Conventional nonspecific immunosuppressive agents, that may be administered in combination with the Therapeutics of the invention include, but are not limited to, steroids, cyclosporine, cyclosporine analogs, cyclophosphamide

methylprednisone, prednisone, azathioprine, FK-506, 15-deoxyspergualin, and other immunosuppressive agents that act by suppressing the function of responding T cells.

In specific embodiments, Therapeutics of the invention are administered in combination with immunosuppressants. Immunosuppressants preparations that may be administered with the Therapeutics of the invention include, but are not limited to, ORTHOCLONE™ (OKT3), SANDIMMUNE™/NEORAL™/SANGDYA™ (cyclosporin), PROGRAF™ (tacrolimus), CELLCEPT™ (mycophenolate), Azathioprine, glucocorticosteroids, and RAPAMUNE™ (sirolimus). In a specific embodiment, immunosuppressants may be used to prevent rejection of organ or bone marrow transplantation.

In an additional embodiment, Therapeutics of the invention are administered alone or in combination with one or more intravenous immune globulin preparations. Intravenous immune globulin preparations that may be administered with the Therapeutics of the invention include, but not limited to, GAMMAR™, IVEEGAM™, SANDOGLOBULIN™, GAMMAGARD S/D™, and GAMIMUNE™. In a specific embodiment, Therapeutics of the invention are administered in combination with intravenous immune globulin preparations in transplantation therapy (e.g., bone marrow transplant).

In an additional embodiment, the Therapeutics of the invention are administered alone or in combination with an anti-inflammatory agent. Anti-inflammatory agents that may be administered with the Therapeutics of the invention include, but are not limited to, glucocorticoids and the nonsteroidal anti-inflammatories, aminoarylcarboxylic acid derivatives, arylacetic acid derivatives, arylbutyric acid derivatives, arylcarboxylic acids, arylpropionic acid derivatives, pyrazoles, pyrazolones, salicylic acid derivatives, thiazinecarboxamides, ϵ -acetamidocaproic acid, S-adenosylmethionine, 3-amino-4-hydroxybutyric acid, amixetrine, bendazac, benzydamine, bucolome, difenpiramide, ditazol, emorfazone, guaiazulene, nabumetone, nimesulide, orgotein, oxaceprol, paranyline, perisoxal, pifoxime, proquazone, proxazole, and tenidap.

In another embodiment, compositions of the invention are administered in

combination with a chemotherapeutic agent. Chemotherapeutic agents that may be administered with the Therapeutics of the invention include, but are not limited to, antibiotic derivatives (e.g., doxorubicin, bleomycin, daunorubicin, and dactinomycin); antiestrogens (e.g., tamoxifen); antimetabolites (e.g., fluorouracil, 5-FU, methotrexate, floxuridine, interferon alpha-2b, glutamic acid, plicamycin, mercaptopurine, and 6-thioguanine); cytotoxic agents (e.g., carmustine, BCNU, lomustine, CCNU, cytosine arabinoside, cyclophosphamide, estramustine, hydroxyurea, procarbazine, mitomycin, busulfan, cis-platin, and vincristine sulfate); hormones (e.g., medroxyprogesterone, estramustine phosphate sodium, ethinyl estradiol, estradiol, megestrol acetate, methyltestosterone, diethylstilbestrol diphosphate, chlorotrianisene, and testolactone); nitrogen mustard derivatives (e.g., mephallen, chorambucil, mechlorethamine (nitrogen mustard) and thiotepa); steroids and combinations (e.g., bethamethasone sodium phosphate); and others (e.g., dicarbazine, asparaginase, mitotane, vincristine sulfate, vinblastine sulfate, and etoposide).

In a specific embodiment, Therapeutics of the invention are administered in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or any combination of the components of CHOP. In another embodiment, Therapeutics of the invention are administered in combination with Rituximab. In a further embodiment, Therapeutics of the invention are administered with Rituxmab and CHOP, or Rituxmab and any combination of the components of CHOP.

In an additional embodiment, the Therapeutics of the invention are administered in combination with cytokines. Cytokines that may be administered with the Therapeutics of the invention include, but are not limited to, IL2, IL3, IL4, IL5, IL6, IL7, IL10, IL12, IL13, IL15, anti-CD40, CD40L, IFN-gamma and TNF-alpha. In another embodiment, Therapeutics of the invention may be administered with any interleukin, including, but not limited to, IL-1alpha, IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IL-19, IL-20, and IL-21.

In an additional embodiment, the Therapeutics of the invention are administered in combination with angiogenic proteins. Angiogenic proteins that may be administered with the Therapeutics of the invention include, but are not limited to, Glioma Derived Growth Factor (GDGF), as disclosed in European Patent Number EP-399816; Platelet Derived Growth Factor-A (PDGF-A), as disclosed in European Patent Number EP-682110; Platelet Derived Growth Factor-B (PDGF-B), as disclosed in European Patent Number EP-282317; Placental Growth Factor (PIGF), as disclosed in International Publication Number WO 92/06194; Placental Growth Factor-2 (PIGF-2), as disclosed in Hauser et al., Growth Factors, 4:259-268 (1993); Vascular Endothelial Growth Factor (VEGF), as disclosed in International Publication Number WO 90/13649; Vascular Endothelial Growth Factor-A (VEGF-A), as disclosed in European Patent Number EP-506477; Vascular Endothelial Growth Factor-2 (VEGF-2), as disclosed in International Publication Number WO 96/39515; Vascular Endothelial Growth Factor B (VEGF-3); Vascular Endothelial Growth Factor B-186 (VEGF-B186), as disclosed in International Publication Number WO 96/26736; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/02543; Vascular Endothelial Growth Factor-D (VEGF-D), as disclosed in International Publication Number WO 98/07832; and Vascular Endothelial Growth Factor-E (VEGF-E), as disclosed in German Patent Number DE19639601. The above mentioned references are incorporated herein by reference herein.

In an additional embodiment, the Therapeutics of the invention are administered in combination with hematopoietic growth factors. Hematopoietic growth factors that may be administered with the Therapeutics of the invention include, but are not limited to, LEUKINE™ (SARGRAMOSTIM™) and NEUPOGEN™ (FILGRASTIM™).

In an additional embodiment, the Therapeutics of the invention are administered in combination with Fibroblast Growth Factors. Fibroblast Growth Factors that may be administered with the Therapeutics of the invention include, but are not limited to, FGF-1, FGF-2, FGF-3, FGF-4, FGF-5, FGF-6, FGF-7, FGF-8,

FGF-9, FGF-10, FGF-11, FGF-12, FGF-13, FGF-14, and FGF-15.

In additional embodiments, the Therapeutics of the invention are administered in combination with other therapeutic or prophylactic regimens, such as, for example, radiation therapy.

5

Example 14: Method of Treating Decreased Levels of the Polypeptide

The present invention relates to a method for treating an individual in need of an increased level of a polypeptide of the invention in the body comprising
10 administering to such an individual a composition comprising a therapeutically effective amount of an agonist of the invention (including polypeptides of the invention). Moreover, it will be appreciated that conditions caused by a decrease in the standard or normal expression level of a polypeptide of the present invention in an individual can be treated by administering the agonist or antagonist of the present
15 invention. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a Therapeutic comprising an amount of the agonist or antagonist to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily
20 dose 0.1-100 ug/kg of the agonist or antagonist for six consecutive days. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 13.

25

Example 15: Method of Treating Increased Levels of the Polypeptide

The present invention also relates to a method of treating an individual in need of a decreased level of a polypeptide of the invention in the body comprising administering to such an individual a composition comprising a therapeutically effective amount of an antagonist of the invention (including polypeptides and
30 antibodies of the invention).

In one example, antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 13.

10 *Example 16: Method of Treatment Using Gene Therapy-Ex Vivo*

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37 degree C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

25 pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set

forth in Example 1 using primers and having appropriate restriction sites and initiation/stop codons, if necessary. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

Example 17: Gene Therapy Using Endogenous Genes Corresponding To

Polynucleotides of the Invention

Another method of gene therapy according to the present invention involves operably associating the endogenous polynucleotide sequence of the invention with a promoter via homologous recombination as described, for example, in U.S. Patent NO: 5,641,670, issued June 24, 1997; International Publication NO: WO 96/29411, published September 26, 1996; International Publication NO: WO 94/12650, published August 4, 1994; Koller et al., *Proc. Natl. Acad. Sci. USA*, 86:8932-8935 (1989); and Zijlstra et al., *Nature*, 342:435-438 (1989). This method involves the activation of a gene which is present in the target cells, but which is not expressed in the cells, or is expressed at a lower level than desired.

Polynucleotide constructs are made which contain a promoter and targeting sequences, which are homologous to the 5' non-coding sequence of endogenous polynucleotide sequence, flanking the promoter. The targeting sequence will be sufficiently near the 5' end of the polynucleotide sequence so the promoter will be operably linked to the endogenous sequence upon homologous recombination. The promoter and the targeting sequences can be amplified using PCR. Preferably, the amplified promoter contains distinct restriction enzyme sites on the 5' and 3' ends. Preferably, the 3' end of the first targeting sequence contains the same restriction enzyme site as the 5' end of the amplified promoter and the 5' end of the second targeting sequence contains the same restriction site as the 3' end of the amplified promoter.

The amplified promoter and the amplified targeting sequences are digested with the appropriate restriction enzymes and subsequently treated with calf intestinal phosphatase. The digested promoter and digested targeting sequences are added together in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The construct is size fractionated on an agarose gel then purified by phenol extraction and ethanol precipitation.

In this Example, the polynucleotide constructs are administered as naked

polynucleotides via electroporation. However, the polynucleotide constructs may also be administered with transfection-facilitating agents, such as liposomes, viral sequences, viral particles, precipitating agents, etc. Such methods of delivery are known in the art.

5 Once the cells are transfected, homologous recombination will take place which results in the promoter being operably linked to the endogenous polynucleotide sequence. This results in the expression of polynucleotide corresponding to the polynucleotide in the cell. Expression may be detected by immunological staining, or any other method known in the art.

10 Fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in DMEM + 10% fetal calf serum. Exponentially growing or early stationary phase fibroblasts are trypsinized and rinsed from the plastic surface with nutrient medium. An aliquot of the cell suspension is removed for counting, and the remaining cells are subjected to centrifugation. The supernatant is aspirated and the pellet is
15 resuspended in 5 ml of electroporation buffer (20 mM HEPES pH 7.3, 137 mM NaCl, 5 mM KCl, 0.7 mM Na₂ HPO₄, 6 mM dextrose). The cells are recentrifuged, the supernatant aspirated, and the cells resuspended in electroporation buffer containing 1 mg/ml acetylated bovine serum albumin. The final cell suspension contains approximately 3×10^6 cells/ml. Electroporation should be performed immediately
20 following resuspension.

 Plasmid DNA is prepared according to standard techniques. For example, to construct a plasmid for targeting to the locus corresponding to the polynucleotide of the invention, plasmid pUC18 (MBI Fermentas, Amherst, NY) is digested with HindIII. The CMV promoter is amplified by PCR with an XbaI site on the 5' end and
25 a BamHI site on the 3'end. Two non-coding sequences are amplified via PCR: one non-coding sequence (fragment 1) is amplified with a HindIII site at the 5' end and an Xba site at the 3'end; the other non-coding sequence (fragment 2) is amplified with a BamHI site at the 5'end and a HindIII site at the 3'end. The CMV promoter and the fragments (1 and 2) are digested with the appropriate enzymes (CMV promoter - XbaI
30 and BamHI; fragment 1 - XbaI; fragment 2 - BamHI) and ligated together. The

resulting ligation product is digested with HindIII, and ligated with the HindIII-digested pUC18 plasmid.

Plasmid DNA is added to a sterile cuvette with a 0.4 cm electrode gap (Bio-Rad). The final DNA concentration is generally at least 120 µg/ml. 0.5 ml of the
5 cell suspension (containing approximately 1.5×10^6 cells) is then added to the cuvette, and the cell suspension and DNA solutions are gently mixed. Electroporation is performed with a Gene-Pulser apparatus (Bio-Rad). Capacitance and voltage are set at 960 µF and 250-300 V, respectively. As voltage increases, cell survival decreases, but the percentage of surviving cells that stably incorporate the introduced DNA into their
10 genome increases dramatically. Given these parameters, a pulse time of approximately 14-20 mSec should be observed.

Electroporated cells are maintained at room temperature for approximately 5 min, and the contents of the cuvette are then gently removed with a sterile transfer pipette. The cells are added directly to 10 ml of prewarmed nutrient media (DMEM
15 with 15% calf serum) in a 10 cm dish and incubated at 37 degree C. The following day, the media is aspirated and replaced with 10 ml of fresh media and incubated for a further 16-24 hours.

The engineered fibroblasts are then injected into the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads. The fibroblasts
20 now produce the protein product. The fibroblasts can then be introduced into a patient as described above.

Example 18: Method of Treatment Using Gene Therapy - In Vivo

25 Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide. The polynucleotide of the present invention may be operatively linked to a promoter
30 or any other genetic elements necessary for the expression of the polypeptide by the

target tissue. Such gene therapy and delivery techniques and methods are known in the art. see. for example, WO90/11092. WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata et al., *Cardiovasc. Res.* 35(3):470-479 (1997); Chao et al., *Pharmacol. Res.* 35(6):517-522 (1997); Wolff, *Neuromuscul. Disord.* 7(5):314-318 (1997); Schwartz et al., *Gene Ther.* 3(5):405-411 (1996); Tsurumi et al., *Circulation* 94(12):3281-3290 (1996) (incorporated herein by reference).

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) *Ann. NY Acad. Sci.* 772:126-139 and Abdallah B. et al. (1995) *Biol. Cell* 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder,

stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same
5 matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and
10 expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

15 For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the
20 tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an
25 aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for
30 polypeptide of the present invention is prepared in accordance with a standard

recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

Example 19: Transgenic Animals

The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e.g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (i.e., polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40:691-698 (1994); Carver et al., Biotechnology (NY) 11:1263-1270 (1993); Wright et al., Biotechnology (NY) 9:830-834 (1991); and Hoppe et al., U.S. Pat. No. 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82:6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56:313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3:1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e.g., Ulmer et al., Science 259:1745 (1993); introducing nucleic acid constructs into embryonic pluripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (Lavitrano et al., Cell 57:717-723 (1989); etc. For a review of such techniques, see Gordon, "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989), which is incorporated by reference herein in its entirety.

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campbell et al., Nature 380:64-66 (1996); Wilmut et al., Nature 385:810-813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, i.e., mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, e.g., head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci. USA 89:6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When

it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265:103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, *in situ* hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to

produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

10 *Example 20: Knock-Out Animals*

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (*E.g.*, see Smithies et al., *Nature* 317:230-234 (1985); Thomas & Capecchi, *Cell* 51:503-512 (1987); Thompson et al., *Cell* 5:313-321 (1989); each of which is incorporated by reference herein in its entirety). For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention *in vivo*. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (*e.g.*, see Thomas & Capecchi 1987 and Thompson 1989, *supra*). However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site *in vivo* using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e.g., knockouts) are administered to a patient *in vivo*. Such cells may be obtained from the patient (i.e.,
5 animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e.g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered *in vitro* using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or
10 endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc. The coding sequence of the polypeptides of the invention can be placed under the
15 control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e.g., in the circulation, or intraperitoneally.

20 Alternatively, the cells can be incorporated into a matrix and implanted in the body, e.g., genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U.S. Patent No. 5,399,349; and Mulligan & Wilson, U.S. Patent No. 5,460,959 each of which is incorporated by
25 reference herein in its entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing
30 for an exchange of components with the immediate extracellular environment, does

not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 22: Assays Detecting Stimulation or Inhibition of B cell Proliferation and Differentiation

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Generation of functional humoral immune responses requires both soluble and cognate signaling between B-lineage cells and their microenvironment. Signals may impart a positive stimulus that allows a B-lineage cell to continue its programmed development, or a negative stimulus that instructs the cell to arrest its current developmental pathway. To date, numerous stimulatory and inhibitory signals have been found to influence B cell responsiveness including IL-2, IL-4, IL-5, IL-6, IL-7, IL10, IL-13, IL-14 and IL-15. Interestingly, these signals are by themselves weak effectors but can, in combination with various co-stimulatory proteins, induce activation, proliferation, differentiation, homing, tolerance and death among B cell populations.

20

One of the best studied classes of B-cell co-stimulatory proteins is the TNF-superfamily. Within this family CD40, CD27, and CD30 along with their respective ligands CD154, CD70, and CD153 have been found to regulate a variety of immune responses. Assays which allow for the detection and/or observation of the proliferation and differentiation of these B-cell populations and their precursors are valuable tools in determining the effects various proteins may have on these B-cell populations in terms of proliferation and differentiation. Listed below are two assays designed to allow for the detection of the differentiation, proliferation, or inhibition of B-cell populations and their precursors.

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In Vitro Assay- Agonists or antagonists of the invention can be assessed for

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its ability to induce activation, proliferation, differentiation or inhibition and/or death in B-cell populations and their precursors. The activity of the agonists or antagonists of the invention on purified human tonsillar B cells, measured qualitatively over the dose range from 0.1 to 10,000 ng/mL, is assessed in a standard B-lymphocyte co-stimulation assay in which purified tonsillar B cells are cultured in the presence of either formalin-fixed *Staphylococcus aureus* Cowan I (SAC) or immobilized anti-human IgM antibody as the priming agent. Second signals such as IL-2 and IL-15 synergize with SAC and IgM crosslinking to elicit B cell proliferation as measured by tritiated-thymidine incorporation. Novel synergizing agents can be readily identified using this assay. The assay involves isolating human tonsillar B cells by magnetic bead (MACS) depletion of CD3-positive cells. The resulting cell population is greater than 95% B cells as assessed by expression of CD45R(B220).

Various dilutions of each sample are placed into individual wells of a 96-well plate to which are added 10^5 B-cells suspended in culture medium (RPMI 1640 containing 10% FBS, 5×10^{-5} M 2ME, 100U/ml penicillin, 10ug/ml streptomycin, and 10^{-5} dilution of SAC) in a total volume of 150ul. Proliferation or inhibition is quantitated by a 20h pulse (1uCi/well) with 3 H-thymidine (6.7 Ci/mM) beginning 72h post factor addition. The positive and negative controls are IL2 and medium respectively.

In Vivo Assay- BALB/c mice are injected (i.p.) twice per day with buffer only, or 2 mg/Kg of agonists or antagonists of the invention, or truncated forms thereof. Mice receive this treatment for 4 consecutive days, at which time they are sacrificed and various tissues and serum collected for analyses. Comparison of H&E sections from normal spleens and spleens treated with agonists or antagonists of the invention identify the results of the activity of the agonists or antagonists on spleen cells, such as the diffusion of peri-arterial lymphatic sheaths, and/or significant increases in the nucleated cellularity of the red pulp regions, which may indicate the activation of the differentiation and proliferation of B-cell populations. Immunohistochemical studies using a B cell marker, anti-CD45R(B220), are used to determine whether any physiological changes to splenic cells, such as splenic

disorganization, are due to increased B-cell representation within loosely defined B-cell zones that infiltrate established T-cell regions.

Flow cytometric analyses of the spleens from mice treated with agonist or antagonist is used to indicate whether the agonists or antagonists specifically
5 increases the proportion of ThB+, CD45R(B220)dull B cells over that which is observed in control mice.

Likewise, a predicted consequence of increased mature B-cell representation in vivo is a relative increase in serum Ig titers. Accordingly, serum IgM and IgA levels are compared between buffer and agonists or antagonists-treated mice.

10 The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

15 *Example 23: T Cell Proliferation Assay*

A CD3-induced proliferation assay is performed on PBMCs and is measured by the uptake of ^3H -thymidine. The assay is performed as follows. Ninety-six well plates are coated with 100 μl /well of mAb to CD3 (HIT3a, Pharmingen) or isotype-
20 matched control mAb (B33.1) overnight at 4 degrees C (1 $\mu\text{g}/\text{ml}$ in .05M bicarbonate buffer, pH 9.5), then washed three times with PBS. PBMC are isolated by F/H gradient centrifugation from human peripheral blood and added to quadruplicate wells (5×10^4 /well) of mAb coated plates in RPMI containing 10% FCS and P/S in the presence of varying concentrations of agonists or antagonists of the invention (total
25 volume 200 μl). Relevant protein buffer and medium alone are controls. After 48 hr. culture at 37 degrees C, plates are spun for 2 min. at 1000 rpm and 100 μl of supernatant is removed and stored -20 degrees C for measurement of IL-2 (or other cytokines) if effect on proliferation is observed. Wells are supplemented with 100 μl of medium containing 0.5 μCi of ^3H -thymidine and cultured at 37 degrees C for 18-24
30 hr. Wells are harvested and incorporation of ^3H -thymidine used as a measure of

proliferation. Anti-CD3 alone is the positive control for proliferation. IL-2 (100 U/ml) is also used as a control which enhances proliferation. Control antibody which does not induce proliferation of T cells is used as the negative controls for the effects of agonists or antagonists of the invention.

- 5 The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

10 *Example 24: Effect of Agonists or Antagonists of the Invention on the Expression of MHC Class II, Costimulatory and Adhesion Molecules and Cell Differentiation of Monocytes and Monocyte-Derived Human Dendritic Cells*

- Dendritic cells are generated by the expansion of proliferating precursors
15 found in the peripheral blood: adherent PBMC or elutriated monocytic fractions are cultured for 7-10 days with GM-CSF (50 ng/ml) and IL-4 (20 ng/ml). These dendritic cells have the characteristic phenotype of immature cells (expression of CD1, CD80, CD86, CD40 and MHC class II antigens). Treatment with activating factors, such as TNF- α , causes a rapid change in surface phenotype (increased expression of MHC
20 class I and II, costimulatory and adhesion molecules, downregulation of FC γ RII, upregulation of CD83). These changes correlate with increased antigen-presenting capacity and with functional maturation of the dendritic cells.

- FACS analysis of surface antigens is performed as follows. Cells are treated
1-3 days with increasing concentrations of agonist or antagonist of the invention or
25 LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degrees C. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

- 30 Effect on the production of cytokines. Cytokines generated by dendritic cells, in

particular IL-12. are important in the initiation of T-cell dependent immune responses. IL-12 strongly influences the development of Th1 helper T-cell immune response, and induces cytotoxic T and NK cell function. An ELISA is used to measure the IL-12 release as follows. Dendritic cells ($10^6/\text{ml}$) are treated with increasing concentrations of agonists or antagonists of the invention for 24 hours. LPS (100 ng/ml) is added to the cell culture as positive control. Supernatants from the cell cultures are then collected and analyzed for IL-12 content using commercial ELISA kit (e.g., R & D Systems (Minneapolis, MN)). The standard protocols provided with the kits are used.

10 Effect on the expression of MHC Class II, costimulatory and adhesion molecules.

Three major families of cell surface antigens can be identified on monocytes: adhesion molecules, molecules involved in antigen presentation, and Fc receptor. Modulation of the expression of MHC class II antigens and other costimulatory molecules, such as B7 and ICAM-1, may result in changes in the antigen presenting capacity of monocytes and ability to induce T cell activation. Increase expression of Fc receptors may correlate with improved monocyte cytotoxic activity, cytokine release and phagocytosis.

FACS analysis is used to examine the surface antigens as follows. Monocytes are treated 1-5 days with increasing concentrations of agonists or antagonists of the invention or LPS (positive control), washed with PBS containing 1% BSA and 0.02 mM sodium azide, and then incubated with 1:20 dilution of appropriate FITC- or PE-labeled monoclonal antibodies for 30 minutes at 4 degreesC. After an additional wash, the labeled cells are analyzed by flow cytometry on a FACScan (Becton Dickinson).

25

Monocyte activation and/or increased survival. Assays for molecules that activate (or alternatively, inactivate) monocytes and/or increase monocyte survival (or alternatively, decrease monocyte survival) are known in the art and may routinely be applied to determine whether a molecule of the invention functions as an inhibitor or activator of monocytes. Agonists or antagonists of the invention can be screened

30

using the three assays described below. For each of these assays, Peripheral blood mononuclear cells (PBMC) are purified from single donor leukopacks (American Red Cross, Baltimore, MD) by centrifugation through a Histopaque gradient (Sigma). Monocytes are isolated from PBMC by counterflow centrifugal elutriation.

5

Monocyte Survival Assay. Human peripheral blood monocytes progressively lose viability when cultured in absence of serum or other stimuli. Their death results from internally regulated process (apoptosis). Addition to the culture of activating factors, such as TNF-alpha dramatically improves cell survival and prevents DNA
10 fragmentation. Propidium iodide (PI) staining is used to measure apoptosis as follows. Monocytes are cultured for 48 hours in polypropylene tubes in serum-free medium (positive control), in the presence of 100 ng/ml TNF-alpha (negative control), and in the presence of varying concentrations of the compound to be tested. Cells are suspended at a concentration of 2×10^6 /ml in PBS containing PI at a final
15 concentration of 5 µg/ml, and then incubated at room temperature for 5 minutes before FACScan analysis. PI uptake has been demonstrated to correlate with DNA fragmentation in this experimental paradigm.

Effect on cytokine release. An important function of monocytes/macrophages is their
20 regulatory activity on other cellular populations of the immune system through the release of cytokines after stimulation. An ELISA to measure cytokine release is performed as follows. Human monocytes are incubated at a density of 5×10^5 cells/ml with increasing concentrations of agonists or antagonists of the invention and under the same conditions, but in the absence of agonists or antagonists. For IL-12
25 production, the cells are primed overnight with IFN (100 U/ml) in presence of agonist or antagonist of the invention. LPS (10 ng/ml) is then added. Conditioned media are collected after 24h and kept frozen until use. Measurement of TNF-alpha, IL-10, MCP-1 and IL-8 is then performed using a commercially available ELISA kit (e. g, R & D Systems (Minneapolis, MN)) and applying the standard protocols provided with
30 the kit.

Oxidative burst. Purified monocytes are plated in 96-w plate at 2×10^5 cell/well. Increasing concentrations of agonists or antagonists of the invention are added to the wells in a total volume of 0.2 ml culture medium (RPMI 1640 + 10% FCS, glutamine and antibiotics). After 3 days incubation, the plates are centrifuged and the medium is removed from the wells. To the macrophage monolayers, 0.2 ml per well of phenol red solution (140 mM NaCl, 10 mM potassium phosphate buffer pH 7.0, 5.5 mM dextrose, 0.56 mM phenol red and 19 U/ml of HRPO) is added, together with the stimulant (200 nM PMA). The plates are incubated at 37°C for 2 hours and the reaction is stopped by adding 20 μ l 1N NaOH per well. The absorbance is read at 610 nm. To calculate the amount of H_2O_2 produced by the macrophages, a standard curve of a H_2O_2 solution of known molarity is performed for each experiment.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 25: Biological Effects of Agonists or Antagonists of the Invention

Astrocyte and Neuronal Assays.

Agonists or antagonists of the invention, expressed in *Escherichia coli* and purified as described above, can be tested for activity in promoting the survival, neurite outgrowth, or phenotypic differentiation of cortical neuronal cells and for inducing the proliferation of glial fibrillary acidic protein immunopositive cells, astrocytes. The selection of cortical cells for the bioassay is based on the prevalent expression of FGF-1 and FGF-2 in cortical structures and on the previously reported enhancement of cortical neuronal survival resulting from FGF-2 treatment. A thymidine incorporation assay, for example, can be used to elucidate an agonist or

antagonist of the invention's activity on these cells.

Moreover, previous reports describing the biological effects of FGF-2 (basic FGF) on cortical or hippocampal neurons *in vitro* have demonstrated increases in both neuron survival and neurite outgrowth (Walicke et al., "Fibroblast growth factor promotes survival of dissociated hippocampal neurons and enhances neurite extension." *Proc. Natl. Acad. Sci. USA* 83:3012-3016. (1986), assay herein incorporated by reference in its entirety). However, reports from experiments done on PC-12 cells suggest that these two responses are not necessarily synonymous and may depend on not only which FGF is being tested but also on which receptor(s) are expressed on the target cells. Using the primary cortical neuronal culture paradigm, the ability of an agonist or antagonist of the invention to induce neurite outgrowth can be compared to the response achieved with FGF-2 using, for example, a thymidine incorporation assay.

15 Fibroblast and endothelial cell assays.

Human lung fibroblasts are obtained from Clonetics (San Diego, CA) and maintained in growth media from Clonetics. Dermal microvascular endothelial cells are obtained from Cell Applications (San Diego, CA). For proliferation assays, the human lung fibroblasts and dermal microvascular endothelial cells can be cultured at 5,000 cells/well in a 96-well plate for one day in growth medium. The cells are then incubated for one day in 0.1% BSA basal medium. After replacing the medium with fresh 0.1% BSA medium, the cells are incubated with the test proteins for 3 days. Alamar Blue (Alamar Biosciences, Sacramento, CA) is added to each well to a final concentration of 10%. The cells are incubated for 4 hr. Cell viability is measured by reading in a CytoFluor fluorescence reader. For the PGE₂ assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or agonists or antagonists of the invention with or without IL-1 α for 24 hours. The

supernatants are collected and assayed for PGE₂ by EIA kit (Cayman, Ann Arbor, MI). For the IL-6 assays, the human lung fibroblasts are cultured at 5,000 cells/well in a 96-well plate for one day. After a medium change to 0.1% BSA basal medium, the cells are incubated with FGF-2 or with or without agonists or antagonists of the invention IL-1 α for 24 hours. The supernatants are collected and assayed for IL-6 by ELISA kit (Endogen, Cambridge, MA).

Human lung fibroblasts are cultured with FGF-2 or agonists or antagonists of the invention for 3 days in basal medium before the addition of Alamar Blue to assess effects on growth of the fibroblasts. FGF-2 should show a stimulation at 10 - 2500 ng/ml which can be used to compare stimulation with agonists or antagonists of the invention.

Parkinson Models.

The loss of motor function in Parkinson's disease is attributed to a deficiency of striatal dopamine resulting from the degeneration of the nigrostriatal dopaminergic projection neurons. An animal model for Parkinson's that has been extensively characterized involves the systemic administration of 1-methyl-4 phenyl 1,2,3,6-tetrahydropyridine (MPTP). In the CNS, MPTP is taken-up by astrocytes and catabolized by monoamine oxidase B to 1-methyl-4-phenyl pyridine (MPP⁺) and released. Subsequently, MPP⁺ is actively accumulated in dopaminergic neurons by the high-affinity reuptake transporter for dopamine. MPP⁺ is then concentrated in mitochondria by the electrochemical gradient and selectively inhibits nicotinamide adenine disphosphate: ubiquinone oxidoreductionase (complex I), thereby interfering with electron transport and eventually generating oxygen radicals.

It has been demonstrated in tissue culture paradigms that FGF-2 (basic FGF) has trophic activity towards nigral dopaminergic neurons (Ferrari et al., Dev. Biol. 1989). Recently, Dr. Unsicker's group has demonstrated that administering FGF-2 in gel foam implants in the striatum results in the near complete protection of nigral dopaminergic neurons from the toxicity associated with MPTP exposure (Otto and

Unsicker, J. Neuroscience, 1990).

Based on the data with FGF-2, agonists or antagonists of the invention can be evaluated to determine whether it has an action similar to that of FGF-2 in enhancing dopaminergic neuronal survival *in vitro* and it can also be tested *in vivo* for protection of dopaminergic neurons in the striatum from the damage associated with MPTP treatment. The potential effect of an agonist or antagonist of the invention is first examined *in vitro* in a dopaminergic neuronal cell culture paradigm. The cultures are prepared by dissecting the midbrain floor plate from gestation day 14 Wistar rat embryos. The tissue is dissociated with trypsin and seeded at a density of 200,000 cells/cm² on polyorthinine-laminin coated glass coverslips. The cells are maintained in Dulbecco's Modified Eagle's medium and F12 medium containing hormonal supplements (N1). The cultures are fixed with paraformaldehyde after 8 days *in vitro* and are processed for tyrosine hydroxylase, a specific marker for dopaminergic neurons, immunohistochemical staining. Dissociated cell cultures are prepared from embryonic rats. The culture medium is changed every third day and the factors are also added at that time.

Since the dopaminergic neurons are isolated from animals at gestation day 14, a developmental time which is past the stage when the dopaminergic precursor cells are proliferating, an increase in the number of tyrosine hydroxylase immunopositive neurons would represent an increase in the number of dopaminergic neurons surviving *in vitro*. Therefore, if an agonist or antagonist of the invention acts to prolong the survival of dopaminergic neurons, it would suggest that the agonist or antagonist may be involved in Parkinson's Disease.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 26: The Effect of Agonists or Antagonists of the Invention on the Growth of

Vascular Endothelial Cells

On day 1, human umbilical vein endothelial cells (HUVEC) are seeded at 2×10^4 cells/35 mm dish density in M199 medium containing 4% fetal bovine serum (FBS), 16 units/ml heparin, and 50 units/ml endothelial cell growth supplements (ECGS, Biotechnology, Inc.). On day 2, the medium is replaced with M199 containing 10% FBS, 8 units/ml heparin. An agonist or antagonist of the invention, and positive controls, such as VEGF and basic FGF (bFGF) are added, at varying concentrations. On days 4 and 6, the medium is replaced. On day 8, cell number is determined with a Coulter Counter.

An increase in the number of HUVEC cells indicates that the compound of the invention may proliferate vascular endothelial cells, while a decrease in the number of HUVEC cell indicates that the compound of the invention inhibits vascular endothelial cells.

The studies described in this example tested activity of a polypeptide of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), agonists, and/or antagonists of the invention.

Example 27: Rat Corneal Wound Healing Model

This animal model shows the effect of an agonist or antagonist of the invention on neovascularization. The experimental protocol includes:

- a) Making a 1-1.5 mm long incision from the center of cornea into the stromal layer.
- b) Inserting a spatula below the lip of the incision facing the outer corner of the eye.
- c) Making a pocket (its base is 1-1.5 mm from the edge of the eye).
- d) Positioning a pellet, containing 50ng- 5ug of an agonist or antagonist of the invention, within the pocket.

e) Treatment with an agonist or antagonist of the invention can also be applied topically to the corneal wounds in a dosage range of 20mg - 500mg (daily treatment for five days).

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

Example 28: Diabetic Mouse and Glucocorticoid-Impaired Wound Healing Models

10

A. Diabetic db+/db+ Mouse Model.

To demonstrate that an agonist or antagonist of the invention accelerates the healing process, the genetically diabetic mouse model of wound healing is used. The full thickness wound healing model in the db+/db+ mouse is a well characterized, clinically relevant and reproducible model of impaired wound healing. Healing of the diabetic wound is dependent on formation of granulation tissue and re-epithelialization rather than contraction (Gartner, M.H. *et al.*, *J. Surg. Res.* 52:389 (1992); Greenhalgh, D.G. *et al.*, *Am. J. Pathol.* 136:1235 (1990)).

The diabetic animals have many of the characteristic features observed in Type II diabetes mellitus. Homozygous (db+/db+) mice are obese in comparison to their normal heterozygous (db+/+m) littermates. Mutant diabetic (db+/db+) mice have a single autosomal recessive mutation on chromosome 4 (db+) (Coleman *et al.* *Proc. Natl. Acad. Sci. USA* 77:283-293 (1982)). Animals show polyphagia, polydipsia and polyuria. Mutant diabetic mice (db+/db+) have elevated blood glucose, increased or normal insulin levels, and suppressed cell-mediated immunity (Mandel *et al.*, *J. Immunol.* 120:1375 (1978); Debray-Sachs, M. *et al.*, *Clin. Exp. Immunol.* 51(1):1-7 (1983); Leiter *et al.*, *Am. J. of Pathol.* 114:46-55 (1985)). Peripheral neuropathy, myocardial complications, and microvascular lesions, basement membrane thickening and glomerular filtration abnormalities have been described in these animals (Norido, F. *et al.*, *Exp. Neurol.* 83(2):221-232 (1984);

Robertson *et al.*, *Diabetes* 29(1):60-67 (1980); Giacomelli *et al.*, *Lab Invest.* 40(4):460-473 (1979); Coleman, D.L., *Diabetes* 31 (Suppl):1-6 (1982)). These homozygous diabetic mice develop hyperglycemia that is resistant to insulin analogous to human type II diabetes (Mandel *et al.*, *J. Immunol.* 120:1375-1377 (1978)).

The characteristics observed in these animals suggests that healing in this model may be similar to the healing observed in human diabetes (Greenhalgh, *et al.*, *Am. J. of Pathol.* 136:1235-1246 (1990)).

Genetically diabetic female C57BL/KsJ (db+/db+) mice and their non-diabetic (db+/+m) heterozygous littermates are used in this study (Jackson Laboratories). The animals are purchased at 6 weeks of age and are 8 weeks old at the beginning of the study. Animals are individually housed and received food and water ad libitum. All manipulations are performed using aseptic techniques. The experiments are conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

Wounding protocol is performed according to previously reported methods (Tsuboi, R. and Rifkin, D.B., *J. Exp. Med.* 172:245-251 (1990)). Briefly, on the day of wounding, animals are anesthetized with an intraperitoneal injection of Avertin (0.01 mg/mL), 2,2,2-tribromoethanol and 2-methyl-2-butanol dissolved in deionized water. The dorsal region of the animal is shaved and the skin washed with 70% ethanol solution and iodine. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is then created using a Keyes tissue punch. Immediately following wounding, the surrounding skin is gently stretched to eliminate wound expansion. The wounds are left open for the duration of the experiment. Application of the treatment is given topically for 5 consecutive days commencing on the day of wounding. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

Wounds are visually examined and photographed at a fixed distance at the day of surgery and at two day intervals thereafter. Wound closure is determined by daily

measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

- 5 An agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for
10 histology and immunohistochemistry. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing. Three groups of 10 animals each (5 diabetic and 5 non-diabetic controls) are evaluated: 1) Vehicle placebo control, 2) untreated group, and 3) treated group. Wound closure is analyzed by measuring the area in the vertical and horizontal axis
15 and obtaining the total square area of the wound. Contraction is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm², the corresponding size of the dermal punch. Calculations are made using the following formula:

20
$$[\text{Open area on day 8}] - [\text{Open area on day 1}] / [\text{Open area on day 1}]$$

Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using a Reichert-Jung microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-
25 sections of bisected wounds. Histologic examination of the wounds are used to assess whether the healing process and the morphologic appearance of the repaired skin is altered by treatment with an agonist or antagonist of the invention. This assessment included verification of the presence of cell accumulation, inflammatory cells, capillaries, fibroblasts, re-epithelialization and epidermal maturity (Greenhalgh, D.G.
30 *et al.*, *Am. J. Pathol.* 136:1235 (1990)). A calibrated lens micrometer is used by a

blinded observer.

Tissue sections are also stained immunohistochemically with a polyclonal rabbit anti-human keratin antibody using ABC Elite detection system. Human skin is used as a positive tissue control while non-immune IgG is used as a negative control.

- 5 Keratinocyte growth is determined by evaluating the extent of reepithelialization of the wound using a calibrated lens micrometer.

Proliferating cell nuclear antigen/cyclin (PCNA) in skin specimens is demonstrated by using anti-PCNA antibody (1:50) with an ABC Elite detection system. Human colon cancer served as a positive tissue control and human brain
10 tissue is used as a negative tissue control. Each specimen included a section with omission of the primary antibody and substitution with non-immune mouse IgG. Ranking of these sections is based on the extent of proliferation on a scale of 0-8, the lower side of the scale reflecting slight proliferation to the higher side reflecting intense proliferation.

- 15 Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

B. Steroid Impaired Rat Model

The inhibition of wound healing by steroids has been well documented in various *in vitro* and *in vivo* systems (Wahl, Glucocorticoids and Wound healing. In: Anti-Inflammatory Steroid Action: Basic and Clinical Aspects. 280-302 (1989); Wahl *et al.*, *J. Immunol.* 115: 476-481 (1975); Werb *et al.*, *J. Exp. Med.* 147:1684-1694 (1978)). Glucocorticoids retard wound healing by inhibiting angiogenesis, decreasing vascular permeability (Ebert *et al.*, *Am. Intern. Med.* 37:701-705 (1952)), fibroblast
25 proliferation, and collagen synthesis (Beck *et al.*, *Growth Factors.* 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978)) and producing a transient reduction of circulating monocytes (Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", In: Antiinflammatory Steroid Action: Basic and Clinical Aspects, Academic Press, New York, pp. 280-302 (1989)). The
30 systemic administration of steroids to impaired wound healing is a well establish

phenomenon in rats (Beck *et al.*, *Growth Factors*, 5: 295-304 (1991); Haynes *et al.*, *J. Clin. Invest.* 61: 703-797 (1978); Wahl, "Glucocorticoids and wound healing", *In: Antiinflammatory Steroid Action: Basic and Clinical Aspects*, Academic Press, New York, pp. 280-302 (1989); Pierce *et al.*, *Proc. Natl. Acad. Sci. USA* 86: 2229-2233 (1989)).

To demonstrate that an agonist or antagonist of the invention can accelerate the healing process, the effects of multiple topical applications of the agonist or antagonist on full thickness excisional skin wounds in rats in which healing has been impaired by the systemic administration of methylprednisolone is assessed.

10 Young adult male Sprague Dawley rats weighing 250-300 g (Charles River Laboratories) are used in this example. The animals are purchased at 8 weeks of age and are 9 weeks old at the beginning of the study. The healing response of rats is impaired by the systemic administration of methylprednisolone (17mg/kg/rat intramuscularly) at the time of wounding. Animals are individually housed and
15 received food and water *ad libitum*. All manipulations are performed using aseptic techniques. This study is conducted according to the rules and guidelines of Human Genome Sciences, Inc. Institutional Animal Care and Use Committee and the Guidelines for the Care and Use of Laboratory Animals.

20 The wounding protocol is followed according to section A, above. On the day of wounding, animals are anesthetized with an intramuscular injection of ketamine (50 mg/kg) and xylazine (5 mg/kg). The dorsal region of the animal is shaved and the skin washed with 70% ethanol and iodine solutions. The surgical area is dried with sterile gauze prior to wounding. An 8 mm full-thickness wound is created using a Keyes tissue punch. The wounds are left open for the duration of the experiment.
25 Applications of the testing materials are given topically once a day for 7 consecutive days commencing on the day of wounding and subsequent to methylprednisolone administration. Prior to treatment, wounds are gently cleansed with sterile saline and gauze sponges.

30 Wounds are visually examined and photographed at a fixed distance at the day of wounding and at the end of treatment. Wound closure is determined by daily

measurement on days 1-5 and on day 8. Wounds are measured horizontally and vertically using a calibrated Jameson caliper. Wounds are considered healed if granulation tissue is no longer visible and the wound is covered by a continuous epithelium.

- 5 The agonist or antagonist of the invention is administered using at a range different doses, from 4mg to 500mg per wound per day for 8 days in vehicle. Vehicle control groups received 50mL of vehicle solution.

 Animals are euthanized on day 8 with an intraperitoneal injection of sodium pentobarbital (300mg/kg). The wounds and surrounding skin are then harvested for
10 histology. Tissue specimens are placed in 10% neutral buffered formalin in tissue cassettes between biopsy sponges for further processing.

 Four groups of 10 animals each (5 with methylprednisolone and 5 without glucocorticoid) are evaluated: 1) Untreated group 2) Vehicle placebo control 3) treated groups.

- 15 Wound closure is analyzed by measuring the area in the vertical and horizontal axis and obtaining the total area of the wound. Closure is then estimated by establishing the differences between the initial wound area (day 0) and that of post treatment (day 8). The wound area on day 1 is 64mm², the corresponding size of the dermal punch. Calculations are made using the following formula:

20

$$[\text{Open area on day 8}] - [\text{Open area on day 1}] / [\text{Open area on day 1}]$$

- Specimens are fixed in 10% buffered formalin and paraffin embedded blocks are sectioned perpendicular to the wound surface (5mm) and cut using an Olympus
25 microtome. Routine hematoxylin-eosin (H&E) staining is performed on cross-sections of bisected wounds. Histologic examination of the wounds allows assessment of whether the healing process and the morphologic appearance of the repaired skin is improved by treatment with an agonist or antagonist of the invention. A calibrated lens micrometer is used by a blinded observer to determine the distance of the wound
30 gap.

Experimental data are analyzed using an unpaired t test. A p value of < 0.05 is considered significant.

The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g.,
5 gene therapy).

Example 29: Lymphadema Animal Model

10 The purpose of this experimental approach is to create an appropriate and consistent lymphedema model for testing the therapeutic effects of an agonist or antagonist of the invention in lymphangiogenesis and re-establishment of the lymphatic circulatory system in the rat hind limb. Effectiveness is measured by swelling volume of the affected limb, quantification of the amount of lymphatic
15 vasculature, total blood plasma protein, and histopathology. Acute lymphedema is observed for 7-10 days. Perhaps more importantly, the chronic progress of the edema is followed for up to 3-4 weeks.

Prior to beginning surgery, blood sample is drawn for protein concentration analysis. Male rats weighing approximately ~350g are dosed with Pentobarbital.
20 Subsequently, the right legs are shaved from knee to hip. The shaved area is swabbed with gauze soaked in 70% EtOH. Blood is drawn for serum total protein testing. Circumference and volumetric measurements are made prior to injecting dye into paws after marking 2 measurement levels (0.5 cm above heel, at mid-pt of dorsal paw). The intradermal dorsum of both right and left paws are injected with 0.05 ml of
25 1% Evan's Blue. Circumference and volumetric measurements are then made following injection of dye into paws.

Using the knee joint as a landmark, a mid-leg inguinal incision is made circumferentially allowing the femoral vessels to be located. Forceps and hemostats are used to dissect and separate the skin flaps. After locating the femoral vessels, the
30 lymphatic vessel that runs along side and underneath the vessel(s) is located. The

main lymphatic vessels in this area are then electrically coagulated or suture ligated.

Using a microscope, muscles in back of the leg (near the semitendinosus and adductors) are bluntly dissected. The popliteal lymph node is then located. The 2 proximal and 2 distal lymphatic vessels and distal blood supply of the popliteal node are then and ligated by suturing. The popliteal lymph node, and any accompanying adipose tissue, is then removed by cutting connective tissues.

Care is taken to control any mild bleeding resulting from this procedure. After lymphatics are occluded, the skin flaps are sealed by using liquid skin (Vetbond) (AJ Buck). The separated skin edges are sealed to the underlying muscle tissue while leaving a gap of ~0.5 cm around the leg. Skin also may be anchored by suturing to underlying muscle when necessary.

To avoid infection, animals are housed individually with mesh (no bedding). Recovering animals are checked daily through the optimal edematous peak, which typically occurred by day 5-7. The plateau edematous peak are then observed. To evaluate the intensity of the lymphedema, the circumference and volumes of 2 designated places on each paw before operation and daily for 7 days are measured. The effect plasma proteins on lymphedema is determined and whether protein analysis is a useful testing perimeter is also investigated. The weights of both control and edematous limbs are evaluated at 2 places. Analysis is performed in a blind manner.

Circumference Measurements: Under brief gas anesthetic to prevent limb movement, a cloth tape is used to measure limb circumference. Measurements are done at the ankle bone and dorsal paw by 2 different people then those 2 readings are averaged. Readings are taken from both control and edematous limbs.

Volumetric Measurements: On the day of surgery, animals are anesthetized with Pentobarbital and are tested prior to surgery. For daily volumetrics animals are under brief halothane anesthetic (rapid immobilization and quick recovery), both legs are shaved and equally marked using waterproof marker on legs. Legs are first dipped in water, then dipped into instrument to each marked level then measured by Buxco edema software(Chen/Victor). Data is recorded by one person, while the other

is dipping the limb to marked area.

Blood-plasma protein measurements: Blood is drawn, spun, and serum separated prior to surgery and then at conclusion for total protein and Ca^{2+} comparison.

- 5 Limb Weight Comparison: After drawing blood, the animal is prepared for tissue collection. The limbs are amputated using a quillitine, then both experimental and control legs are cut at the ligature and weighed. A second weighing is done as the tibio-cacaneal joint is disarticulated and the foot is weighed.

- 10 Histological Preparations: The transverse muscle located behind the knee (popliteal) area is dissected and arranged in a metal mold, filled with freezeGel, dipped into cold methylbutane, placed into labeled sample bags at -80°C until sectioning. Upon sectioning, the muscle is observed under fluorescent microscopy for lymphatics..

- 15 The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

- 20 *Example 30: Suppression of TNF alpha-induced adhesion molecule expression by a Agonist or Antagonist of the Invention*

- 25 The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an
- 30

inflammatory response. The local concentration of cytokines and growth factor participate in the modulation of the expression of these CAMs.

Tumor necrosis factor alpha (TNF- α), a potent proinflammatory cytokine, is a stimulator of all three CAMs on endothelial cells and may be involved in a wide variety of inflammatory responses, often resulting in a pathological outcome.

The potential of an agonist or antagonist of the invention to mediate a suppression of TNF- α induced CAM expression can be examined. A modified ELISA assay which uses ECs as a solid phase absorbent is employed to measure the amount of CAM expression on TNF- α treated ECs when co-stimulated with a member of the FGF family of proteins.

To perform the experiment, human umbilical vein endothelial cell (HUVEC) cultures are obtained from pooled cord harvests and maintained in growth medium (EGM-2; Clonetics, San Diego, CA) supplemented with 10% FCS and 1% penicillin/streptomycin in a 37 degree C humidified incubator containing 5% CO₂.

HUVECs are seeded in 96-well plates at concentrations of 1×10^4 cells/well in EGM medium at 37 degree C for 18-24 hrs or until confluent. The monolayers are subsequently washed 3 times with a serum-free solution of RPMI-1640 supplemented with 100 U/ml penicillin and 100 mg/ml streptomycin, and treated with a given cytokine and/or growth factor(s) for 24 h at 37 degree C. Following incubation, the cells are then evaluated for CAM expression.

Human Umbilical Vein Endothelial cells (HUVECs) are grown in a standard 96 well plate to confluence. Growth medium is removed from the cells and replaced with 90 μ l of 199 Medium (10% FBS). Samples for testing and positive or negative controls are added to the plate in triplicate (in 10 μ l volumes). Plates are incubated at 37 degree C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 μ l of 0.1% paraformaldehyde-PBS(with Ca⁺⁺ and Mg⁺⁺) is added to each well. Plates are held at 4°C for 30 min.

Fixative is then removed from the wells and wells are washed 1X with PBS(+Ca,Mg)+0.5% BSA and drained. Do not allow the wells to dry. Add 10 μ l of

diluted primary antibody to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 µg/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA.

5 Then add 20 µl of diluted ExtrAvidin-Alkaline Phosphatase (1:5,000 dilution) to each well and incubated at 37°C for 30 min. Wells are washed X3 with PBS(+Ca,Mg)+0.5% BSA. 1 tablet of p-Nitrophenol Phosphate pNPP is dissolved in 5 ml of glycine buffer (pH 10.4). 100 µl of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution
10 of the ExtrAvidin-Alkaline Phosphatase in glycine buffer: $1:5,000 (10^0) > 10^{-0.5} > 10^{-1} > 10^{-1.5}$. 5 µl of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 µl of pNPP reagent must then be added to each of the standard wells. The plate must be incubated at 37°C for 4h. A volume of 50 µl of 3M NaOH is added to all wells. The results are quantified on a
15 plate reader at 405 nm. The background subtraction option is used on blank wells filled with glycine buffer only. The template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

20 The studies described in this example tested activity of agonists or antagonists of the invention. However, one skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides or polypeptides of the invention (e.g., gene therapy).

25 *Example 31: Production Of Polypeptide of the Invention For High-Throughput Screening Assays*

 The following protocol produces a supernatant containing polypeptide of the present invention to be tested. This supernatant can then be used in the Screening Assays described in Examples 33-42.

30 First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution

(1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel).

- 5 Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at 2×10^5 cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine
10 (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an
15 expression vector containing a polynucleotide insert, produced by the methods described in Examples 8-10, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well.
20 As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates
25 of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a 12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37 degree C for 6 hours.

30 While cells are incubating, prepare appropriate media, either 1%BSA in

DMEM with 1x penstrep, or HGS CHO-5 media (116.6 mg/L of CaCl_2 (anhyd); 0.00130 mg/L $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$; 0.050 mg/L of $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$; 0.417 mg/L of $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$; 311.80 mg/L of KCl; 28.64 mg/L of MgCl_2 ; 48.84 mg/L of MgSO_4 ; 6995.50 mg/L of NaCl; 2400.0 mg/L of NaHCO_3 ; 62.50 mg/L of $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$;
5 71.02 mg/L of Na_2HPO_4 ; .4320 mg/L of $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$; .002 mg/L of Arachidonic Acid ; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of
10 Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine- H_2O ; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL- H_2O ; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL- H_2O ; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-
15 Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalanine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tyrosine-2Na-2 H_2O ; and 99.65 mg/ml of L-Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic
20 Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; 0.680 mg/L of Vitamin B₁₂; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of
25 Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal Acetate. Adjust osmolarity to 327 mOsm) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM

for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person
5 B adds 1.5ml appropriate media to each well. Incubate at 37 degree C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 33-40.

10 It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide of the present invention directly (e.g., as a secreted protein) or by polypeptide of the present invention inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of
15 identifying the protein in the supernatant characterized by an activity in a particular assay.

Example 32: Construction of GAS Reporter Construct

20 One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

25 GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class 1, cells after treatment with
30 IL-12. Stat5 was originally called mammary growth factor, but has been found at

higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN- α , IFN- γ , and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:920)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

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		<u>JAKs</u>				<u>STATS GAS(elements) or</u>
<u>ISRE</u>						
<u>Ligand</u>	<u>tyk2</u>	<u>Jak1</u>	<u>Jak2</u>	<u>Jak3</u>		
5 <u>IFN family</u>						
IFN-a/B	+	+	-	-	1,2,3	ISRE
IFN-g (IRF1>Lys6>IFP)		+	+	-	1	GAS
IL-10	+	?	?	-	1,3	
10 <u>gp130 family</u>						
IL-6 (Pleiotrohic) (IRF1>Lys6>IFP)	+	+	+	?	1,3	GAS
IL-11 (Pleiotrohic)	?	+	?	?	1,3	
15 OnM (Pleiotrohic)	?	+	+	?	1,3	
LIF (Pleiotrohic)	?	+	+	?	1,3	
CNTF (Pleiotrohic)	-/+	+	+	?	1,3	
G-CSF (Pleiotrohic)	?	+	?	?	1,3	
IL-12 (Pleiotrohic)	+	-	+	+	1,3	
20 <u>g-C family</u>						
IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
IL-4 (lymph/myeloid) >>Ly6)(IgH)	-	+	-	+	6	GAS (IRF1 = IFP
25 IL-7 (lymphocytes)	-	+	-	+	5	GAS
IL-9 (lymphocytes)	-	+	-	+	5	GAS
IL-13 (lymphocyte)	-	+	?	?	6	GAS
IL-15	?	+	?	+	5	GAS
30 <u>gp140 family</u>						
IL-3 (myeloid) (IRF1>IFP>>Ly6)	-	-	+	-	5	GAS
IL-5 (myeloid)	-	-	+	-	5	GAS

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GM-CSF (myeloid)	-	-	+	-	5	GAS
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Growth hormone family

	GH	?	-	+	-	5	
5	PRL	?	+/-	+	-	1,3,5	
	EPO	?	-	+	-	5	GAS(B-
	CAS>IRF1=IFP>>Ly6)						

Receptor Tyrosine Kinases

10	EGF	?	+	+	-	1,3	GAS (IRF1)
	PDGF	?	+	+	-	1,3	
	CSF-1	?	+	+	-	1,3	GAS (not IRF1)

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 33-34, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

5':GCGCCTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCC
GAAATGATTTCCCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:921)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:922)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAA
TGATTTCCCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCC
CCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCGCCCCATTCT
CCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCC
TCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTA
GGCTTTTGCAAAAAAGCTT:3' (SEQ ID NO:923)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol

acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and
5 XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-
10 SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding
15 as described in Examples 33-34.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 35 and 36. However, many other promoters can be substituted using the protocols described
20 in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

25

Example 33: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, and determining whether supernate containing a polypeptide of the invention
30 proliferates and/or differentiates T-cells. T-cell activity is assessed using the

GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC
5 Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately
10 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells
15 containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies) with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

20 During the incubation period, count cell concentration, spin down the required number of cells (10^7 per transfection), and resuspend in OPTI-MEM to a final concentration of 10^7 cells/ml. Then add 1ml of 1×10^7 cells in OPTI-MEM to T25 flask and incubate at 37 degree C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

25 The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Gentamicin, and 1% Pen-Strep. These cells are treated with supernatants containing polypeptide of the present invention or polypeptide of the present invention induced polypeptides as produced by the protocol described in Example 31.

30 On the day of treatment with the supernatant, the cells should be washed and

resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

- 5 Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

- After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12
10 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

- The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul
15 samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20 degree C until SEAP assays are performed according to Example 37. The plates containing the remaining treated cells are placed at 4 degree C and serve as a source of material for repeating the assay on a specific well if desired.

- 20 As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

 The above protocol may be used in the generation of both transient, as well as, stable transfected cells, which would be apparent to those of skill in the art.

25

Example 34: High-Throughput Screening Assay Identifying Myeloid Activity

- The following protocol is used to assess myeloid activity of polypeptide of the present invention by determining whether polypeptide of the present invention
30 proliferates and/or differentiates myeloid cells. Myeloid cell activity is assessed using

the GAS/SEAP/Neo construct produced in Example 32. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

- 5 To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 32, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2×10^7 U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml
10 penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 1 mM MgCl_2 , and 675 uM CaCl_2 . Incubate at 37 degrees C for 45 min.

- 15 Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37 degree C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

- 20 These cells are tested by harvesting 1×10^8 cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of 5×10^5 cells/ml. Plate 200 ul cells per well in the 96-well plate (or 1×10^5 cells/well).

- Add 50 ul of the supernatant prepared by the protocol described in Example
25 31. Incubate at 37 degree C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 37.

- 30 *Example 35: High-Throughput Screening Assay Identifying Neuronal Activity.*

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed by polypeptide of the present invention.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat pheochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells by polypeptide of the present invention can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO: 924)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO: 925)

Using the GAS:SEAP/Neo vector produced in Example 32, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and

allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and
5 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 31. EGR-SEAP/PC12 stable cells are obtained by
10 growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS
15 (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as 5×10^5
20 cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to 1×10^5 cells/well). Add 50 ul supernatant produced by Example 31, 37 degree C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over
25 fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 37.

Example 36: High-Throughput Screening Assay for T-cell Activity

30 NF-KB (Nuclear Factor KB) is a transcription factor activated by a wide

variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-KB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- KB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- KB is retained in the cytoplasm with I-KB (Inhibitor KB). However, upon stimulation, I- KB is phosphorylated and degraded, causing NF- KB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- KB include IL-2, IL-6, GM-CSF, ICAM-1 and class I MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-KB promoter element are used to screen the supernatants produced in Example 31. Activators or inhibitors of NF-KB would be useful in treating, preventing, and/or diagnosing diseases. For example, inhibitors of NF-KB could be used to treat those diseases related to the acute or chronic activation of NF-KB, such as rheumatoid arthritis.

To construct a vector containing the NF-KB promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF-KB binding site (GGGGACTTTCCC) (SEQ ID NO:926), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC
TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:927)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTGGCAAAGCCTAGGC:3' (SEQ ID NO:922)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene)

Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGGACTTTCC
ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCCTAACTCCGCCC
5 ATCCCGCCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGA
CTAATTTTTTTTTATTTATGCAGAGGCCGAGGCCGCTCGGCCTCTGAGCTA
TTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAA
GCTT:3' (SEQ ID NO:928)

Next, replace the SV40 minimal promoter element present in the pSEAP2-
10 promoter plasmid (Clontech) with this NF-KB/SV40 fragment using XhoI and
HindIII. However, this vector does not contain a neomycin resistance gene, and
therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF-KB/SV40/SEAP
cassette is removed from the above NF-KB/SEAP vector using restriction enzymes
15 Sall and NotI, and inserted into a vector containing neomycin resistance. Particularly,
the NF-KB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the
GFP gene, after restricting pGFP-1 with Sall and NotI.

Once NF-KB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are
created and maintained according to the protocol described in Example 33. Similarly,
20 the method for assaying supernatants with these stable Jurkat T-cells is also described
in Example 33. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to
wells H9, H10, and H11, with a 5-10 fold activation typically observed.

Example 37: Assay for SEAP Activity

25

As a reporter molecule for the assays described in Examples 33-36, SEAP
activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the
following general procedure. The Tropix Phospho-light Kit supplies the Dilution,
Assay, and Reaction Buffers used below.

30 Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 ul of 2.5x

dilution buffer into Optiplates containing 35 ul of a supernatant. Seal the plates with a plastic sealer and incubate at 65 degree C for 30 min. Separate the Optiplates to avoid uneven heating.

- Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 ml Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 ul Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

Reaction Buffer Formulation:

15

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6
23	125	6.25

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24	130	6.5
25	135	6.75
26	140	7
27	145	7.25
28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

Example 38: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants
5 which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to
10 measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-4 (Molecular Probes, Inc.; catalog no. F-14202), used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star
15 black 96-well plate with clear bottom. The plate is incubated in a CO₂ incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-4 is made in 10% pluronic acid DMSO. To load the cells with fluo-4, 50 ul of 12 ug/ml fluo-4 is added to each well. The plate
20 is incubated at 37 degrees C in a CO₂ incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to $2-5 \times 10^6$ cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-4 solution in 10% pluronic acid DMSO is added to each ml of cell suspension.
25 The tube is then placed in a 37 degrees C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1×10^6 cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley Cell Wash with 200 ul, followed by an aspiration step to 100 ul final volume.

30 For a non-cell based assay, each well contains a fluorescent molecule, such as

fluo-4 . The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event caused by the a molecule, either polypeptide of the present invention or a molecule induced by polypeptide of the present invention, which has resulted in an increase in the intracellular Ca^{++} concentration.

10

Example 40: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase (RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, identifying whether polypeptide of the present invention or a molecule induced by polypeptide of the present invention is capable of activating tyrosine kinase signal transduction pathways is of interest. Therefore, the following protocol

30

is designed to identify such molecules capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed with PBS and stored at 4 degree C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 31, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na₃VO₄, 2 mM Na₄P₂O₇ and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4

degree C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

5 Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for
10 a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg₂⁺ (5mM ATP/50mM MgCl₂), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl₂, 5 mM MnCl₂,
15 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30 degree C for 2 min. Initial the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA and place the reactions on ice.

20 Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37 degree C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-
25 POD(0.5u/ml)) to each well and incubate at 37 degree C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound
30 peroxidase activity is quantitated using an ELISA reader and reflects the level of

tyrosine kinase activity.

Example 41: High-Throughput Screening Assay Identifying Phosphorylation Activity

5 As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 40, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other
10 molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

 Specifically, assay plates are made by coating the wells of a 96-well ELISA
15 plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody
20 detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4 degree C until use.

 A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants
25 obtained in Example 31 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

 After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit)
30 antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the

Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased
5 fluorescent signal over background indicates a phosphorylation by polypeptide of the present invention or a molecule induced by polypeptide of the present invention.

Example 42: Assay for the Stimulation of Bone Marrow CD34+ Cell Proliferation

10 This assay is based on the ability of human CD34+ to proliferate in the presence of hematopoietic growth factors and evaluates the ability of isolated polypeptides expressed in mammalian cells to stimulate proliferation of CD34+ cells.

It has been previously shown that most mature precursors will respond to only a single signal. More immature precursors require at least two signals to respond.
15 Therefore, to test the effect of polypeptides on hematopoietic activity of a wide range of progenitor cells, the assay contains a given polypeptide in the presence or absence of other hematopoietic growth factors. Isolated cells are cultured for 5 days in the presence of Stem Cell Factor (SCF) in combination with tested sample. SCF alone has a very limited effect on the proliferation of bone marrow (BM) cells, acting in
20 such conditions only as a "survival" factor. However, combined with any factor exhibiting stimulatory effect on these cells (e.g., IL-3), SCF will cause a synergistic effect. Therefore, if the tested polypeptide has a stimulatory effect on a hematopoietic progenitors, such activity can be easily detected. Since normal BM cells have a low level of cycling cells, it is likely that any inhibitory effect of a given polypeptide, or
25 agonists or antagonists thereof, might not be detected. Accordingly, assays for an inhibitory effect on progenitors is preferably tested in cells that are first subjected to *in vitro* stimulation with SCF+IL+3, and then contacted with the compound that is being evaluated for inhibition of such induced proliferation.

Briefly, CD34+ cells are isolated using methods known in the art. The cells
30 are thawed and resuspended in medium (QBSF 60 serum-free medium with 1% L-

glutamine (500ml) Quality Biological, Inc., Gaithersburg, MD Cat# 160-204-101). After several gentle centrifugation steps at 200 x g, cells are allowed to rest for one hour. The cell count is adjusted to 2.5×10^5 cells/ml. During this time, 100 μ l of sterile water is added to the peripheral wells of a 96-well plate. The cytokines that
5 can be tested with a given polypeptide in this assay is rhSCF (R&D Systems, Minneapolis, MN, Cat# 255-SC) at 50 ng/ml alone and in combination with rhSCF and rhIL-3 (R&D Systems, Minneapolis, MN, Cat# 203-ML) at 30 ng/ml. After one hour, 10 μ l of prepared cytokines, 50 μ l of the supernatants prepared in Example 31 (supernatants at 1:2 dilution = 50 μ l) and 20 μ l of diluted cells are added to the media
10 which is already present in the wells to allow for a final total volume of 100 μ l. The plates are then placed in a 37°C/5% CO₂ incubator for five days.

Eighteen hours before the assay is harvested, 0.5 μ Ci/well of [3H] Thymidine is added in a 10 μ l volume to each well to determine the proliferation rate. The experiment is terminated by harvesting the cells from each 96-well plate to a filtermat
15 using the Tomtec Harvester 96. After harvesting, the filtermats are dried, trimmed and placed into OmniFilter assemblies consisting of one OmniFilter plate and one OmniFilter Tray. 60 μ l Microscint is added to each well and the plate sealed with TopSeal-A press-on sealing film. A bar code 15 sticker is affixed to the first plate for counting. The sealed plates is then loaded and the level of radioactivity determined
20 via the Packard Top Count and the printed data collected for analysis. The level of radioactivity reflects the amount of cell proliferation.

The studies described in this example test the activity of a given polypeptide to stimulate bone marrow CD34+ cell proliferation. One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene
25 therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof. As a nonlimiting example, potential antagonists tested in this assay would be expected to inhibit cell proliferation in the presence of cytokines and/or to increase the inhibition of cell proliferation in the presence of cytokines and a given polypeptide. In contrast, potential agonists tested in this assay would be expected to enhance cell
30 proliferation and/or to decrease the inhibition of cell proliferation in the presence of

cytokines and a given polypeptide.

The ability of a gene to stimulate the proliferation of bone marrow CD34+ cells indicates that polynucleotides and polypeptides corresponding to the gene are useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and
5 "Infectious Disease" sections above, and elsewhere herein.

Example 43: Assay for Extracellular Matrix Enhanced Cell Response (EMECR)

10 The objective of the Extracellular Matrix Enhanced Cell Response (EMECR) assay is to identify gene products (e.g., isolated polypeptides) that act on the hematopoietic stem cells in the context of the extracellular matrix (ECM) induced signal.

Cells respond to the regulatory factors in the context of signal(s) received from
15 the surrounding microenvironment. For example, fibroblasts, and endothelial and epithelial stem cells fail to replicate in the absence of signals from the ECM. Hematopoietic stem cells can undergo self-renewal in the bone marrow, but not in *in vitro* suspension culture. The ability of stem cells to undergo self-renewal *in vitro* is dependent upon their interaction with the stromal cells and the ECM protein
20 fibronectin (fn). Adhesion of cells to fn is mediated by the $\alpha_5\beta_1$ and $\alpha_4\beta_1$ integrin receptors, which are expressed by human and mouse hematopoietic stem cells. The factor(s) which integrate with the ECM environment and responsible for stimulating stem cell self-renewal has not yet been identified. Discovery of such factors should be of great interest in gene therapy and bone marrow transplant applications

25 Briefly, polystyrene, non tissue culture treated, 96-well plates are coated with fn fragment at a coating concentration of $0.2 \mu\text{g}/\text{cm}^2$. Mouse bone marrow cells are plated (1,000 cells/well) in 0.2 ml of serum-free medium. Cells cultured in the presence of IL-3 (5 ng/ml) + SCF (50 ng/ml) would serve as the positive control, conditions under which little self-renewal but pronounced differentiation of the stem

cells is to be expected. Gene products of the invention (e.g., including, but not limited to, polynucleotides and polypeptides of the present invention, and supernatants produced in Example 31), are tested with appropriate negative controls in the presence and absence of SCF(5.0 ng/ml), where test factor supernates represent 10% of the total assay volume. The plated cells are then allowed to grow by incubating in a low oxygen environment (5% CO₂, 7% O₂, and 88% N₂) tissue culture incubator for 7 days. The number of proliferating cells within the wells is then quantitated by measuring thymidine incorporation into cellular DNA. Verification of the positive hits in the assay will require phenotypic characterization of the cells, which can be accomplished by scaling up of the culture system and using appropriate antibody reagents against cell surface antigens and FACSscan.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

If a particular polypeptide of the present invention is found to be a stimulator of hematopoietic progenitors, polynucleotides and polypeptides corresponding to the gene encoding said polypeptide may be useful for the diagnosis and treatment of disorders affecting the immune system and hematopoiesis. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections above, and elsewhere herein. The gene product may also be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Additionally, the polynucleotides and/or polypeptides of the gene of interest and/or agonists and/or antagonists thereof, may also be employed to inhibit the proliferation and differentiation of hematopoietic cells and therefore may be employed to protect bone marrow stem cells from chemotherapeutic agents during chemotherapy. This antiproliferative effect may allow administration of higher doses of chemotherapeutic agents and, therefore, more effective chemotherapeutic treatment.

Moreover, polynucleotides and polypeptides corresponding to the gene of

interest may also be useful for the treatment and diagnosis of hematopoietic related disorders such as, for example, anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex-vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia.

Example 44: Human Dermal Fibroblast and Aortic Smooth Muscle Cell Proliferation

The polypeptide of interest is added to cultures of normal human dermal fibroblasts (NHDF) and human aortic smooth muscle cells (AoSMC) and two co-assays are performed with each sample. The first assay examines the effect of the polypeptide of interest on the proliferation of normal human dermal fibroblasts (NHDF) or aortic smooth muscle cells (AoSMC). Aberrant growth of fibroblasts or smooth muscle cells is a part of several pathological processes, including fibrosis, and restenosis. The second assay examines IL6 production by both NHDF and SMC. IL6 production is an indication of functional activation. Activated cells will have increased production of a number of cytokines and other factors, which can result in a proinflammatory or immunomodulatory outcome. Assays are run with and without co-TNF α stimulation, in order to check for costimulatory or inhibitory activity.

Briefly, on day 1, 96-well black plates are set up with 1000 cells/well (NHDF) or 2000 cells/well (AoSMC) in 100 μ l culture media. NHDF culture media contains: Clonetics FB basal media, 1mg/ml hFGF, 5mg/ml insulin, 50mg/ml gentamycin, 2%FBS, while AoSMC culture media contains Clonetics SM basal media, 0.5 μ g/ml hEGF, 5mg/ml insulin, 1 μ g/ml hFGF, 50mg/ml gentamycin, 50 μ g/ml Amphotericin B, 5%FBS. After incubation at 37°C for at least 4-5 hours, culture media is aspirated and replaced with growth arrest media. Growth arrest media for NHDF contains fibroblast basal media, 50mg/ml gentamycin, 2% FBS, while growth arrest media for AoSMC contains SM basal media, 50mg/ml gentamycin, 50 μ g/ml Amphotericin B, 0.4% FBS. Incubate at 37°C until day 2.

On day 2, serial dilutions and templates of the polypeptide of interest are designed such that they always include media controls and known-protein controls. For both stimulation and inhibition experiments, proteins are diluted in growth arrest media. For inhibition experiments, TNF α is added to a final concentration of 2ng/ml (NHDF) or 5ng/ml (AoSMC). Add 1/3 vol media containing controls or polypeptides of the present invention and incubate at 37°C/5% CO₂ until day 5.

Transfer 60 μ l from each well to another labeled 96-well plate, cover with a plate-sealer, and store at 4°C until Day 6 (for IL6 ELISA). To the remaining 100 μ l in the cell culture plate, aseptically add Alamar Blue in an amount equal to 10% of the culture volume (10 μ l). Return plates to incubator for 3 to 4 hours. Then measure fluorescence with excitation at 530nm and emission at 590nm using the CytoFluor. This yields the growth stimulation/inhibition data.

On day 5, the IL6 ELISA is performed by coating a 96 well plate with 50-100 μ l/well of Anti-Human IL6 Monoclonal antibody diluted in PBS, pH 7.4, incubate ON at room temperature.

On day 6, empty the plates into the sink and blot on paper towels. Prepare Assay Buffer containing PBS with 4% BSA. Block the plates with 200 μ l/well of Pierce Super Block blocking buffer in PBS for 1-2 hr and then wash plates with wash buffer (PBS, 0.05% Tween-20). Blot plates on paper towels. Then add 50 μ l/well of diluted Anti-Human IL-6 Monoclonal, Biotin-labeled antibody at 0.50 mg/ml. Make dilutions of IL-6 stock in media (30, 10, 3, 1, 0.3, 0 ng/ml). Add duplicate samples to top row of plate. Cover the plates and incubate for 2 hours at RT on shaker. Plates are washed with wash buffer and blotted on paper towels. Dilute EU-labeled Streptavidin 1:1000 in Assay buffer, and add 100 μ l/well. Cover the plate and incubate 1 h at RT. Plates are again washed with wash buffer and blotted on paper towels. Add 100 μ l/well of Enhancement Solution and shake for 5 minutes. Read the plate on the Wallac DELFIA Fluorometer. Readings from triplicate samples in each assay are tabulated and averaged.

A positive result in this assay suggests AoSMC cell proliferation and that the polypeptide of the present invention may be involved in dermal fibroblast

proliferation and/or smooth muscle cell proliferation. A positive result also suggests many potential uses of polypeptides, polynucleotides, agonists and/or antagonists of the polynucleotide/polypeptide of the present invention which gives a positive result. For example, inflammation and immune responses, wound healing, and angiogenesis, as detailed throughout this specification. Particularly, polypeptides of the present invention and polynucleotides of the present invention may be used in wound healing and dermal regeneration, as well as the promotion of vasculogenesis, both of the blood vessels and lymphatics. The growth of vessels can be used in the treatment of, for example, cardiovascular diseases. Additionally, antagonists of polypeptides and polynucleotides of the invention may be useful in treating diseases, disorders, and/or conditions which involve angiogenesis by acting as an anti-vascular (e.g., anti-angiogenesis). These diseases, disorders, and/or conditions are known in the art and/or are described herein, such as, for example, malignancies, solid tumors, benign tumors, for example hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas; arteriosclerotic plaques; ocular angiogenic diseases, for example, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, retinoblastoma, uveitis and Pterygia (abnormal blood vessel growth) of the eye; rheumatoid arthritis; psoriasis; delayed wound healing; endometriosis; vasculogenesis; granulations; hypertrophic scars (keloids); nonunion fractures; scleroderma; trachoma; vascular adhesions; myocardial angiogenesis; coronary collaterals; cerebral collaterals; arteriovenous malformations; ischemic limb angiogenesis; Osler-Webber Syndrome; plaque neovascularization; telangiectasia; hemophilic joints; angiofibroma; fibromuscular dysplasia; wound granulation; Crohn's disease; and atherosclerosis. Moreover, antagonists of polypeptides and polynucleotides of the invention may be useful in treating anti-hyperproliferative diseases and/or anti-inflammatory known in the art and/or described herein.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

Example 45: Cellular Adhesion Molecule (CAM) Expression on Endothelial Cells

5 The recruitment of lymphocytes to areas of inflammation and angiogenesis involves specific receptor-ligand interactions between cell surface adhesion molecules (CAMs) on lymphocytes and the vascular endothelium. The adhesion process, in both normal and pathological settings, follows a multi-step cascade that involves intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1
10 (VCAM-1), and endothelial leukocyte adhesion molecule-1 (E-selectin) expression on endothelial cells (EC). The expression of these molecules and others on the vascular endothelium determines the efficiency with which leukocytes may adhere to the local vasculature and extravasate into the local tissue during the development of an inflammatory response. The local concentration of cytokines and growth factor
15 participate in the modulation of the expression of these CAMs.

Briefly, endothelial cells (e.g., Human Umbilical Vein Endothelial cells (HUVECs)) are grown in a standard 96 well plate to confluence, growth medium is removed from the cells and replaced with 100 µl of 199 Medium (10% fetal bovine serum (FBS)). Samples for testing and positive or negative controls are added to the
20 plate in triplicate (in 10 µl volumes). Plates are then incubated at 37°C for either 5 h (selectin and integrin expression) or 24 h (integrin expression only). Plates are aspirated to remove medium and 100 µl of 0.1% paraformaldehyde-PBS(with Ca⁺⁺ and Mg⁺⁺) is added to each well. Plates are held at 4°C for 30 min. Fixative is removed from the wells and wells are washed 1X with PBS(+Ca,Mg) + 0.5% BSA
25 and drained. 10 µl of diluted primary antibody is added to the test and control wells. Anti-ICAM-1-Biotin, Anti-VCAM-1-Biotin and Anti-E-selectin-Biotin are used at a concentration of 10 µg/ml (1:10 dilution of 0.1 mg/ml stock antibody). Cells are incubated at 37°C for 30 min. in a humidified environment. Wells are washed three times with PBS(+Ca,Mg) + 0.5% BSA. 20 µl of diluted ExtrAvidin-Alkaline
30 Phosphotase (1:5,000 dilution, referred to herein as the working dilution) are added to

each well and incubated at 37°C for 30 min. Wells are washed three times with PBS(+Ca.Mg)+0.5% BSA. Dissolve 1 tablet of p-Nitrophenol Phosphate pNPP per 5 ml of glycine buffer (pH 10.4). 100 µl of pNPP substrate in glycine buffer is added to each test well. Standard wells in triplicate are prepared from the working dilution of the ExtrAvidin-Alkaline Phosphatase in glycine buffer: 1:5,000 (10^0) > $10^{-0.5}$ > 10^{-1} > $10^{-1.5}$. 5 µl of each dilution is added to triplicate wells and the resulting AP content in each well is 5.50 ng, 1.74 ng, 0.55 ng, 0.18 ng. 100 µl of pNPP reagent is then added to each of the standard wells. The plate is incubated at 37°C for 4h. A volume of 50 µl of 3M NaOH is added to all wells. The plate is read on a plate reader at 405 nm using the background subtraction option on blank wells filled with glycine buffer only. Additionally, the template is set up to indicate the concentration of AP-conjugate in each standard well [5.50 ng; 1.74 ng; 0.55 ng; 0.18 ng]. Results are indicated as amount of bound AP-conjugate in each sample.

15 *Example 46: Alamar Blue Endothelial Cells Proliferation Assay*

This assay may be used to quantitatively determine protein mediated inhibition of bFGF-induced proliferation of Bovine Lymphatic Endothelial Cells (LECs), Bovine Aortic Endothelial Cells (BAECs) or Human Microvascular Uterine Myometrial Cells (UTMECs). This assay incorporates a fluorometric growth indicator based on detection of metabolic activity. A standard Alamar Blue Proliferation Assay is prepared in EGM-2MV with 10 ng /ml of bFGF added as a source of endothelial cell stimulation. This assay may be used with a variety of endothelial cells with slight changes in growth medium and cell concentration. Dilutions of the protein batches to be tested are diluted as appropriate. Serum-free medium (GIBCO SFM) without bFGF is used as a non-stimulated control and Angiostatin or TSP-1 are included as a known inhibitory controls.

Briefly, LEC, BAECs or UTMECs are seeded in growth media at a density of 5000 to 2000 cells/well in a 96 well plate and placed at 37-C overnight. After the overnight incubation of the cells, the growth media is removed and replaced with

GIBCO EC-SFM. The cells are treated with the appropriate dilutions of the protein of interest or control protein sample(s) (prepared in SFM) in triplicate wells with additional bFGF to a concentration of 10 ng/ ml. Once the cells have been treated with the samples, the plate(s) is/are placed back in the 37° C incubator for three days.

- 5 After three days 10 ml of stock alamar blue (Biosource Cat# DAL1100) is added to each well and the plate(s) is/are placed back in the 37°C incubator for four hours. The plate(s) are then read at 530nm excitation and 590nm emission using the CytoFluor fluorescence reader. Direct output is recorded in relative fluorescence units.

- 10 Alamar blue is an oxidation-reduction indicator that both fluoresces and changes color in response to chemical reduction of growth medium resulting from cell growth. As cells grow in culture, innate metabolic activity results in a chemical reduction of the immediate surrounding environment. Reduction related to growth causes the indicator to change from oxidized (non-fluorescent blue) form to reduced (fluorescent red) form. i.e. stimulated proliferation will produce a stronger signal and
- 15 inhibited proliferation will produce a weaker signal and the total signal is proportional to the total number of cells as well as their metabolic activity. The background level of activity is observed with the starvation medium alone. This is compared to the output observed from the positive control samples (bFGF in growth medium) and protein dilutions.

20

Example 47: Detection of Inhibition of a Mixed Lymphocyte Reaction

- This assay can be used to detect and evaluate inhibition of a Mixed Lymphocyte Reaction (MLR) by gene products (e.g., isolated polypeptides).
- 25 Inhibition of a MLR may be due to a direct effect on cell proliferation and viability, modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, or modulation of cytokine production by accessory cells. Multiple cells may be targeted by these polypeptides since the peripheral blood mononuclear fraction used in this assay includes T. B and

natural killer lymphocytes, as well as monocytes and dendritic cells.

Polypeptides of interest found to inhibit the MLR may find application in diseases associated with lymphocyte and monocyte activation or proliferation. These include, but are not limited to, diseases such as asthma, arthritis, diabetes, inflammatory skin conditions, psoriasis, eczema, systemic lupus erythematosus, multiple sclerosis, glomerulonephritis, inflammatory bowel disease, crohn's disease, ulcerative colitis, arteriosclerosis, cirrhosis, graft vs. host disease, host vs. graft disease, hepatitis, leukemia and lymphoma.

Briefly, PBMCs from human donors are purified by density gradient centrifugation using Lymphocyte Separation Medium (LSM[®], density 1.0770 g/ml, Organon Teknika Corporation, West Chester, PA). PBMCs from two donors are adjusted to 2×10^6 cells/ml in RPMI-1640 (Life Technologies, Grand Island, NY) supplemented with 10% FCS and 2 mM glutamine. PBMCs from a third donor is adjusted to 2×10^5 cells/ml. Fifty microliters of PBMCs from each donor is added to wells of a 96-well round bottom microtiter plate. Dilutions of test materials (50 μ l) is added in triplicate to microtiter wells. Test samples (of the protein of interest) are added for final dilution of 1:4; rhIL-2 (R&D Systems, Minneapolis, MN, catalog number 202-IL) is added to a final concentration of 1 μ g/ml; anti-CD4 mAb (R&D Systems, clone 34930.11, catalog number MAB379) is added to a final concentration of 10 μ g/ml. Cells are cultured for 7-8 days at 37°C in 5% CO₂, and 1 μ C of [³H] thymidine is added to wells for the last 16 hrs of culture. Cells are harvested and thymidine incorporation determined using a Packard TopCount. Data is expressed as the mean and standard deviation of triplicate determinations.

Samples of the protein of interest are screened in separate experiments and compared to the negative control treatment, anti-CD4 mAb, which inhibits proliferation of lymphocytes and the positive control treatment, IL-2 (either as recombinant material or supernatant), which enhances proliferation of lymphocytes.

One skilled in the art could easily modify the exemplified studies to test the activity of polynucleotides (e.g., gene therapy), antibodies, agonists, and/or antagonists and fragments and variants thereof.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

- 5 The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both
- 10 incorporated herein by reference in their entireties. Moreover, the hard copy of and the corresponding computer readable form of the Sequence Listing of Serial No. 60/124,270 are also incorporated herein by reference in their entireties.

Applicant's or agent's file reference number	PA105PCT	International application/ reference number	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT	
Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209059
C. ADDITIONAL INDICATIONS (leave blank if not applicable)	
This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
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ATCC Deposit No. 209059**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209059

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application?	UNASSIGNED
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A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209060
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
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ATCC Deposit No. 209060**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209060

DENMARK

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SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	434 PA105PCT	International application: UNASSIGNED
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B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209061
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
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ATCC Deposit No. 209061**CANADA**

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NORWAY

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FINLAND

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UNITED KINGDOM

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Page 2

ATCC Deposit No. 209061

DENMARK

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NETHERLANDS

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437

Applicant's or agent's file reference number	PA105PCT	International application I	700 007 UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209062
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
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<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 209062**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209062

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PA105PCT	International application:	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209063
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

Form PCT/RO/134 (July 1992)

ATCC Deposit No. 209063**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 209063

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

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443

Applicant's or agent's file reference number	PA105PCT	International application ?	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209064
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

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<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit N . 209064**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2**ATCC Deposit No. 209064****DENMARK**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	446 PA105PCT	International application UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209065
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
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For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

Form PCT/RO/134 (July 1992)

ATCC Deposit No. 209065**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 209065

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

ATCC Deposit No. 209066**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Applicant's or agent's file reference number	449 PA105PCT	International application N	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209066
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
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<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

Page 2

ATCC Deposit No. 209066

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	452 PA105PCT	International application N°	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209067
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
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For International Bureau use only
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Authorized officer

ATCC Deposit No. 209067**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

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Page 2
ATCC Deposit No. 209067

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application N	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209068
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 209068**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 209068

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application N	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 20 May 1997	Accession Number 209069
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 209069**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209069

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PA105PCT	International application No.	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 12 January 1998	Accession Number 209579
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 209579**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 209579

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application No.	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>10801 University Boulevard</u> <u>Manassas, Virginia 20110-2209</u> <u>United States of America</u>	
Date of deposit <u>12 January 1998</u>	Accession Number <u>209578</u>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
<u>Europe</u> In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit") 	
For receiving Office use only <input type="checkbox"/> This sheet was received with the international application Authorized officer	For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer

ATCC Deposit No. 209578**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 209578

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application No	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 16 July 1998	Accession Number 203067
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 203067**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 203067

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PA105PCT	470 International application No.	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution <u>American Type Culture Collection</u>	
Address of depositary institution (including postal code and country) <u>10801 University Boulevard</u> <u>Manassas, Virginia 20110-2209</u> <u>United States of America</u>	
Date of deposit <u>16 July 1998</u>	Accession Number <u>203068</u>
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 203068**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 203068

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application N°	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 1 February 1999	Accession Number 203609
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only <input type="checkbox"/> This sheet was received with the international application Authorized officer	For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer
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ATCC Deposit No. 203609**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 203609

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application N°	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 1 February 1999	Accession Number 203610
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 203610**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. 203610

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file reference number	PA105PCT	International application N°	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 17 November 1998	Accession Number 203485
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. 203485**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. 203485

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

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Applicant's or agent's file reference number	PA105PCT	International application N	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 18 June 1999	Accession Number PTA-252
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. PTA-252**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

ATCC Deposit No. PTA-252

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

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NETHERLANDS

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Applicant's or agent's file reference number	PA105PCT	International application No.	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 18 June 1999	Accession Number PTA-253
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	

For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. PTA-253**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

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UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2
ATCC Deposit No. PTA-253

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

488

Applicant's or agent's file reference number	PA105PCT	International application No.	UNASSIGNED
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INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>71</u> . line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 22 December 1999	Accession Number PTA-1081
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
Europe In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
For receiving Office use only	For International Bureau use only
<input type="checkbox"/> This sheet was received with the international application	<input type="checkbox"/> This sheet was received by the International Bureau on:
Authorized officer	Authorized officer

ATCC Deposit No. PTA-1081**CANADA**

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

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ATCC Deposit No. PTA-1081

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
- 5 (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- 10 (c) a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO:X or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (d) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- 15 (e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- 20 (f) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X, having biological activity;
- (g) a polynucleotide which is a variant of SEQ ID NO:X;
- 25 (h) a polynucleotide which is an allelic variant of SEQ ID NO:X;
- (i) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
- (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide
- 30

sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

5

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

10

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

15

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

20

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

25

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

30

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least
5 95% identical to a sequence selected from the group consisting of:
- (a) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
 - (b) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone, having biological activity;
 - 10 (c) a polypeptide domain of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
 - (d) a polypeptide epitope of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
 - (e) a full length protein of SEQ ID NO:Y or of the sequence encoded by the
15 cDNA included in the related cDNA clone;
 - (f) a variant of SEQ ID NO:Y;
 - (g) an allelic variant of SEQ ID NO:Y; or
 - (h) a species homologue of the SEQ ID NO:Y.
- 20 12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
13. An isolated antibody that binds specifically to the isolated polypeptide
25 of claim 11.
14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
- 30 15. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

5 16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

10

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

15 (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

20 (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

25 20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

30

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
22. A method of identifying an activity in a biological assay, wherein the method comprises:
- 5 (a) expressing SEQ ID NO:X in a cell;
- (b) isolating the supernatant;
- (c) detecting an activity in a biological assay; and
- (d) identifying the protein in the supernatant having the activity.
- 10 23. The product produced by the method of claim 20.

SEQUENCE LISTING

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Steve Ruben

<120> Human Pancreas and Pancreatic Cancer Associated Gene Sequences and
Polypeptides

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<210> 11

<211> 847

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (766)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (795)

<223> n equals a,t,g, or c

<400> 11

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gatgatcgtt cgtccgaccg gaggggtgat gaccggcgat actgtggcag ctacagacgc 360
aacgattata gccgggatcg gggagatgcc tactatgaca cagactatcg gcattcctat 420
gaatatcagc gggagaacag cagttaccgc agccagcgca magccggaga agcacagacg 480

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gcgggargarg cgcacggarc atttagccgy tcattcttcgg tgagtgccag cccaggccct 540
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<210> 12

<211> 506

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (416)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (486)

<223> n equals a,t,g, or c

<400> 12

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ccctcagttc cgtctccggc gcggctacct gccccgtttt ccctgtgagt tgacctgtc 180
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tgcgtnccaa actcgaacct ctccgc 506

<210> 13

<211> 267

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (259)

<223> n equals a,t,g, or c

<400> 13

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aattttttta aaaaaatttg tgtgtctctg ctctactata cactggtgtg tccctctgcc 180
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aatcacagct cactgcagnc ttgtcct 267

<210> 14
<211> 919
<212> DNA
<213> Homo sapiens

<400> 14
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<210> 15
<211> 2559
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2543)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2544)
<223> n equals a,t,g, or c

<400> 15
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<210> 16

<211> 1504

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (665)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1503)

<223> n equals a,t,g, or c

<400> 16

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aaatttggtt ctcagcccca aaatactgat tgaattggrrg acaattacaa ggactctctg 120
gccaaaaacc cttgaagagg ccccgtagaagg gaggcagtga ggagcttttg attgctgacc 180

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tgtgtcgtac caccacagaa tgtgcaactgg rggctgtgcc agatgcctgg gggggaccct 240
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aagcgggtgc ttgatgatct tccctgcgct ggtgttcttg ggcctgaaga acaatgactg 420
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aana 1504

<210> 17

<211> 833

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (160)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (258)

<223> n equals a,t,g, or c

<400> 17

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gacttgtagc gcttcggggc agacagcaaa gggaaactggn caccactact gggagaacaa 180
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caggaagatg ggcagagact tkagtggcga ttacctccag cacagagacg tgccaggcgg 720
tggtggcgct cggggcgaga tgctgccctt ctttgacsa agcctggcct cttgcttggc 780
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<210> 18

<211> 643

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (103)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (572)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (613)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (643)

<223> n equals a,t,g, or c

<400> 18

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ccattgaagc cagttccgta tgggctggac ctggactgcg gantccctgg caccaccagag 120
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ggcctgccc ggcggtacc atgtgtaccg gttggaaggc actccctggt gtaatctgag 480
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ggagtgcctt gccctcaaca gcaactggg tnttttctgc agacaaggac ctcaatagtt 600
ctgatgtcca canttttgca gcctcagtta gactttggg ccn 643

<210> 19

<211> 340

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (262)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (333)

<223> n equals a,t,g, or c

<400> 19

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ctgggaatgt agcttctttg tgcccatggt ggataggacc ccagattgts atcctgacca 180
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ctgcagcgcc tgaaacctgg gnggcaagac caagcccga caacccttgc agagtgcct 300
tgaagatgat gacaagccct gttccagtca canccagaag 340
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<210> 20

<211> 673

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<400> 20

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ccgcggctga caccctcgct cgcagtttgt tcgcagtta ctgcacacc agtttcccc 180
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acattagttt ccg 673
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<210> 21

<211> 415

<212> DNA

<213> Homo sapiens

<400> 21

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aattcggcac gagctgaatt atgtttaaat ttattgtagg atgctgatct tctggacaat 60
cacacttttc ctgctgggag cagccaaagg aaaagaagtt tgctatgagg acctcgggtg 120
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cttttttgac actgagccct ggggcgggac agcaatcagg cccctgaaaa ttctcccctg 180
gagccctgag aagatcggca cccgcttcct gctgtacacc aatgaaaacc caaacaactt 240
tcaaattctc ctctctctg atccatcaac aattgaggca tcaaattttc aaatggacag 300
aaagaccggg ttcacatcc atgggtttca tagacaaagg ggatgagagc ttgggtgaca 360
gacatgtgca agaaactttt tcgggggttg aggaggtgaa ctgcatttgc gttgg 415

<210> 22

<211> 633

<212> DNA

<213> Homo sapiens

<400> 22

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gaactgcac tgctgggact ggaagaaggc ctccaagcc acctacacac aggtgccaa 180
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atgtgattca caggatgca gctcccctga tccattctt gggttttgga acgaaccaac 480
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atgccctgtc tcagatcgtg gatctagatg gcatctgggc gggaaccggg gacttttttg 600
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<210> 23

<211> 2423

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (12)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (18)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (54)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2409)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2422)

<223> n equals a,t,g, or c

<400> 23

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tcaaagcaaa gctctttact ttccccttgg ttctcataac tctgtgatmt tgctctcggg 2400
gcttcmaant cakccaagtc cng 2423

```

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<210> 24
<211> 384
<212> DNA
<213> Homo sapiens

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<220>
<221> misc feature
<222> (357)
<223> n equals a,t,g, or c

```

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<400> 24
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aacacagttg aagaaggaaa gtggcgatgg acctcatccc aaatttggcg gtggaaacct 120
ggcttctcct ggctgtcagc ctggtgctcc tctatctata tgggaccctg acacatggac 180
ttttaagag actggaatt ccagggccca cacctctgcc ttgttggga aatgttttgt 240
cctatcgtca ggtctcttgg aaatttgaca cagagtgtga taaaaagtat ggaaaaatgt 300
gggggtgagt attctgaaaa cctccattgg atagacctgc tactgtgagg aggttanccc 360
atgcagagat ctctggccag ttgt 384

```

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<210> 25
<211> 900
<212> DNA
<213> Homo sapiens

```

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<220>
<221> misc feature
<222> (11)
<223> n equals a,t,g, or c

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```

<220>
<221> misc feature
<222> (880)
<223> n equals a,t,g, or c

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<400> 25
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ggccaacttc accaagccca cagccgacgc gccctcgctg ctgcagcatg acgaggtgga 120
gacctacttc catgagtttg gccacgtgat gcaccagctc tgctcccagg cggagttcgc 180
catgttcagc gggaccacag tggagcggga ctttgtggag gcgccgtcgc agatgctgga 240
gaactgggtg tgggagcagg agccgctgct gcggatgttc gcggcactac cgcacaggca 300
gcgccgtgcc ccgggagctc ctggagaagc tcattgagtc ccggcaggcc aacacaggcc 360
tcttcaacct gcgccagatc gtcctcgcca aggtggacca ggccctgcac acgcaracgg 420
acgcagacct cgccgaggag tatgcgcggc tctgccagga gatcctcggg gtcccggcca 480
cgccagggaac caacatgcct gcaaccttcg gccatctggc aggtggctac gacgccagc 540
actacgggta cctgtggagc gaggtgtatt ccatggacat gttccacacg cgcttcaagc 600
aggagggtgt cctgaacagc aaggttggca tggattacag aagctgcacg ctgagacccg 660

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gcggttccga ggatgccagc gccatgctga ggcgcttcct gggccgtgac cccaagcagg 720
acgccttcct cctgagcaag gggctgcagg tcgggggctg cgagcccag cgcagctctg 780
gytgaggcct ggcattgcga ctgcccakty tgggcytgcg ctcccgccgc cctgggtgctt 840
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<210> 26

<211> 1322

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (363)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (366)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1321)

<223> n equals a,t,g, or c

<400> 26

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gaagacagca tgtacacagc cattccccag agtggctctc cattccccag ctcatgtcag 120
gatccaggcc tgcatgtgtg gcgggtggag aagctgaagc cgggtgcctgt ggcgcaagag 180
aaccaggggcg tcttcttctc gggggactcc tacctagtgc tgcacaatgg cccagaagag 240
gtttcccatc tgacactgtg gataggccag cagtcattcc gggatgagca gggggcctgt 300
gccgtgctgg ctgtgcacct caacacgctg ctgggagagc ggcctgtgca gcaccgcag 360
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gaaggtggtg tggagtcagc atttcacaag acctccacag gagccccagc tgccatcaag 480
aaactctacc aggtgaaggg gaagaagaac atccgtgcc aagagcgggc actgaactgg 540
gacagcttca aactgggga ctgcttcatc ctggacctgg gccagaacat ctctgcctgg 600
tgtggtggaa agtccaacat cctggaacgc aacaaggcga gggacctggc cctggccatc 660
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gctgagatga tccaggctct gggccccaag cctgctctga aggagggcaa ccctgaggaa 780
gacctcacag ctgacaaggc aaatgcccag gccgcagctc tgtataaggt ctctgatgcc 840
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cccatcttca agcaattttt caaggactgg aaatgagggg gggcgtcttc ctgccccatg 1140
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ng 1322

<210> 27

<211> 457
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (432)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (435)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (454)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (457)
<223> n equals a,t,g, or c

<400> 27
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atactctcca atctattagc aaaaatcaga gtaaaataca gaggaaaggc actgctttct 120
gttaattgat ttaacatgca tgaattagct ccctctgagt tccaggcact atgctgagag 180
tacaaagaag acacaagtct gctttcaagc aactcactgt gaaagtgttt ttgaagggag 240
gaacagaaat gagacccta tctttcccta taaaaacaac atttttactg tcttttgcct 300
gccaatctgt atttgaaacc attggacact gattctctgg sctgggactt tggcattgat 360
gggtttctgc ctttcttctc agcctctgcc tctattgcat ttattaaact gcattgtgtg 420
caaaaaaaaa anaanaaaaa aaaaaagggg gggncn 457

<210> 28
<211> 596
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (538)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (583)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (593)

<223> n equals a,t,g, or c

<400> 28

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cgcggcgccg ccctcgggtgc ggcacccccg gctcagagga ctctttgctg tcccgcaaga 60
tgcggatgct gctggcgctc ctggccctct ccgcggcgcg ccacggcgag tgcagagtca 120
cactggtgct acgaggttca agccgagtcc tccaactacc cctgcttggg gccagtcaag 180
tgggggtgaa actgccagaa ggaccgccag tccccatca acatcgtcac caccaaggca 240
aaggtggaca aaaaactggg acgcttcttc ttctctggct acgataagaa gcaaactggg 300
actgtccaaa ataacgggca ctcagtgatg atgttgctgg agaacaaggc cagcatttct 360
ggaggaggac tgcccgcccc ataccaggcc aaacagttgc acctgcactg gtccgacttg 420
ccatataagg gctcggagca cagcctcgat kgggaagcat ttgccatggg agatgcacat 480
agttacatga gaaagagaag gggacatccg aggaatgtga aagaggccca ggaccctnaa 540
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```

<210> 29

<211> 436

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (64)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (372)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (410)

<223> n equals a,t,g, or c

<400> 29

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ccaaagaggg gttgmtctct cttcacctrc tctgttctac agcacactac cagaagacag 60
cagnaatagaa aagcattttac ttgtggctg gattatttgt aatgctggta caaggcagct 120
ggcaacggtc cttcaagac acagaggaga aatccagatc attctcagct tcccgaggcag 180
accactcag tgatcctrat cagatgamcg aggacaagcg ccattcacag ggcacattca 240
ccagtgacta cagcaagtat ctggactcca ggcgtgccca agattttgtg cagtggttga 300
tgaataccaa gaggaacagg aataacattg ccaaactgca cgggtgaattt tgagagacat 360
gctggaaggg gncctttttac cagtgggtga agtttcttat ttgggaaggn caagctgccc 420
aagggattca ttgctt 436

```

<210> 30

<211> 1314

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature
<222> (572)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1177)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1284)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1295)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1306)
<223> n equals a,t,g, or c

<400> 30
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gcttggaacac tgagccaagc agacaagcaa agcaagccag gacacacccat cctgccccag 120
gcccagcttc tctcctgcct tccaacgcca tggggagcaa tctcagcccc caactctgcc 180
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ccattggcac aaggaaagtg ggcagccagt accgccttga agacagcgtc acctaccact 720
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ggttgggcca gatggacgtt cccntccttg aaggnttggg aaccgncacc cgcc 1314

<210> 31
<211> 1467
<212> DNA

<213> Homo sapiens

<400> 31

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tagacaagct ggacaagggt tcctgggaag aggtgaagaa tgagatgggt ggagagaagg 180
gccttgcacc tgaggtggct gaccgcattg gggactatgt ccagcaacat ggtgggggat 240
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cttccccagc agaccaatgt agggatggaa aaggagagaa aacagtaaac ttgtgacctt 1380
gaggttcttg tctccagcgt tccacctgcg gcttgggagc ttctcctcgg gaggcagccc 1440
ccgtacatta cgcaccccg cgaacttt 1467
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<210> 32

<211> 2346

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2346)

<223> n equals a,t,g, or c

<400> 32

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gagagacccg gccaaggctt ttgtgcccag gactgttatg attgggggca aggcagcgcc 120
cggttaccac atggccaagc tgatcatcaa gttggtcacc tccatcggcg acgtcgtcaa 180
tcatgacca gttgtgggtg acaggttgaa agtgccttc ctggagaact accgtgtgtc 240
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cgaggcctca ggcacaggca acatgaagtt catgctcaac ggggccctca ccatcggcac 360
catggacggc gccaacgtgg agatggccga ggaggcsggg gccgagaacc tcttcattct 420
cggcctgcgg gtggaggatg tcgaggcctt ggaccggaag ggtacaatg ccaggagata 480
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tcccaaggag ccagactgct tcaaggacat cgtgaacatg ctgatgcacc atgacaggtt 600
caagggtgtt gcagactatg aagcctacat gcagtgccag gcacagggtg accagctgta 660
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ccggaacccc aaggagtgga ccaagaaggt catcaggaac atcgctgct cgggcaagtt 720
ctccagtgac cggaccatca cggagtatgc acgggagatc tggggtgtgg agccctccga 780
cctgcagatc ccgcccccca acatcccccg ggactaggca caccctgcct tggcgggacc 840
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gggggn
2346

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<210> 33

<211> 459

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (388)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (394)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (428)

<223> n equals a,t,g, or c

<400> 33

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tcgacccacg cgtccgagag acagtcacac cagctgcccc tagtggggct cttactgttt 60
tcttttattc caagccaact atgcgagatt tgtgaggtaa gtgaagaaaa ctacatccgc 120
ctaaaacctc tgttgaatac aatgatccag tcaaactata acaggggaac cagcgctgtc 180
aatgttgtgt tgccccctcaa acttggttga atccagatcc aaacctgat gcaaaagatg 240
atccaacaaa tcaaatataa tgtgaaaagc agattgtcag atgtaagctc gggagagytt 300
gccttgatta tactggcttt gggagtatgt cgtaacgctg aggaaaactt aatatatgat 360
taccacctga tcgacaagyt agraatatnaa attnccargc agaaattgga aaatwtggga 420
ggcacacnat gggcactccc ctgacttact acttcccag 459

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<210> 34

<211> 629

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (607)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (613)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (617)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (621)

<223> n equals a,t,g, or c

<400> 34

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gttggacttt aatcttaccg atccagaaaa tgggcctgtt cttgatgatt ctctacaaa 60
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agacctcagc ctgcatgtcg ccaccactga aaaggacctg ctgattgtcc gatcccagaa 180
tgataagttc aacgttagcc tcacagtcaa aaatacaaaag gacagtgcct ataacaccag 240
gacaatagtg cattattctc caaatctagt tttttcagga attgaggcta tccaaaaaga 300
cagtttgtga tctaatacata atatcacatg taaagttgga tatcccttcc tgagaagagg 360
agagatggta actttcaaaa tattgtttca gtttaacaca tcctatctca tgggaaaatg 420
tgaccattta ttttaagtga caagtggaca gcgarggaac ctccctgaaac ccttlytgat 480
aatgtagtaa acatttsytw tcccgggtaa aatwtggaag ttgggctaca gttttacagy 540
tctgcaagtg grwtaccaca tttcaatggc cggccatgga gacagtcccc ggaagtttat 600
taattcnacc gngngancat ngggaaagg 629

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<210> 35

<211> 918

<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (918)
<223> n equals a,t,g, or c

<400> 35
atggcagcgc cgtggctgcc accagcacca tcaacacacc ctttggagcg atggtgtatt 60
caccacggac aggcattcatc ctcaacaacg agctcctgga cttatgagag cgatgcccc 120
gggggtccgg caccaccccc tcacctgtga gtggagacag ggtgggtgga gctcccgaa 180
gtgctggccc ccagttccag gcgagcggtc cccatcctcc atggtgccct ccattctgat 240
caacaaagcc caggggtcga agctagtgtat tggcggggct ggcggggagc tcatcatctc 300
tgctgtggcc caggcatcat gagcaagctg tggcttggct ttgacctgag agcggccatt 360
gcagccccca tcctgcatgt caacagcaag ggctgtgtgg agtacgagcc caacttcagc 420
caggagggtgc agaggggact ccaagaccgt ggccagaacc agaccagag gcccttcttc 480
ctgaacgtgg tccaggctgt gtcccaggag ggggcctgtg tgtacgccgt ctcggaacctg 540
aggaagagtg gggagggcgc aggcactactaa gacactgtct tggccagagc tgaagtctgg 600
ccccaccatg agtcctgtgt ccaggccgga catggctggg ggaccaacta ctctggcagg 660
atctggaccc ctggcagggg agtccagctg agagtggaag aggtggcggg gaccagctgg 720
gcagatgaga gctgagcctc atccctaacc ccctttcca gagcccctgg tggctctgaa 780
ccggccccctc tatccctccg caggcctctt gcctggggcc actctcccac cctctcgatc 840
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aaaaaaaaaa aaaaaaan 918

<210> 36
<211> 802
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (659)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (677)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (684)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (736)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (763)

<223> n equals a,t,g, or c

<400> 36

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tgccctccac agtcggggta gcagctcctc ctcacacagc tcatctgtca ggcggggcag 60
ctcctacagc tcttccatga gcacaggagg aggtggtgca ggctccctgg gtgcaggcgg 120
tgcccttggg gaagctgcag gagacagggg tccctatggc actgacatcg gccaggcgg 180
aggctatggg gcagcagcag aaggcggcat gtatgctggc aatggcggac tattgggagc 240
tgactttgct ggagatctgg attacaatga gctggctgtg aggggtgtcag agagcatgca 300
gcgtcagggg ctactgcaag ggatggccta cactgtccag ggcccaccag gccagcctgg 360
gccacagggg ccaccggga tcagcaaggt cttctctgcc tacagcaacg tgactkcggg 420
cctcatggac ttcttccaaa cttatggagc cattcaagga cccctgggc aaaaaggaga 480
gatgggact ccaggaccca aaggtgacag gggccctgct gggccaccag gtcctcctgg 540
gccacctggc cttctgagga cacaagggag aaaaaggaga caaaggttga ccaagtctat 600
gctgggagga gaaggagaag aagttattgg ctgtcaaccg ttgagctagc catgggcang 660
acagctcctg ggaccangtc ttentaatgc tgtggcatta ggtccaagtc tccagaggtg 720
aaagtggatc tgtcangtct tactgagaca gcacagccaa ctnagtagca acatttggtt 780
tagtctggaa catatatact tt                                     802

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<210> 37

<211> 2093

<212> DNA

<213> Homo sapiens

<400> 37

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gtcctccagg aatccctggc cagcctgggc taaagggtct accaggaccc caaggacctc 60
aaggcttacc aggtccaact ggccctccag gagatcctgg acgcaatgga ctccctggct 120
ttgatgggtg aggagggcgc aaaggagacc caggctctgcc aggacagcca ggtaccctgt 180
gtttggatgg tccccctggc ccagatggat tgcaaggctc cccaggctcc cctggaacct 240
cctctgttgc acatggattt cttattacac gccacagcca gacaacggat gcaccacaat 300
gccacagggg aacacttcag gtctatgaag gcttttctct cctgtatgta caaggaaata 360
aaagagccca cgggtcaagac ttggggacgg ctggcagctg ccttcgtcgc ttagtagcca 420
tgcccttcat gttctgcaac atcaataatg tttgcaactt tgcttcaaga aatgactatt 480
cttactggct ctctaccca gagcccatgc caatgagcat gcaaccccta aagggccaga 540
gcatccagcc attcattagt cgatgtgcag tatgtgaagc tccagctgtg gtgatcgcag 600
ttcacagtca gacgatccag attccccatt gtccctcagg atgggattct ctgtggattg 660
gttattcctt catgatgcat acaagtgcag gggcagaagg ctcagggtcaa gccctagcct 720
cccctgggtc ctgcttgga grgttctgtt cagctccctt catcgaatgt catgggaggg 780
gtacctgtaa ctactatgcc aactcctaca gcttttggct ggcaactgta gatgtgtcag 840
acatgttcag taaacctcag tcagaaacgc tgaaagcagg agacttgagg acacgaatta 900
gccgatgtca agtgtgcatg aagaggacat aacattttga agaattcctt ttgtgtttta 960
aaatgtgata tatatatata taaaattcct aggatgcagt gtctcattgt ccccaacttt 1020
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catgaagatt cagatgtacc tcagcaatgc gccagagcaa agtctctatt atttttctac 1140
taaagaaata aggaagtga tttacttttt ggggtccagaa tgactttctc caagaattat 1200
aagatgaaaa ttatatattt tgcccagtta ctaaaatgg acattaaaaa ttcaattaag 1260
agargagtca cattgagtaa aataaaagac tgcagtttgt gggaagaatt atttttcacg 1320
gtgctactaa tcctgctgta tcccgggttt taaatataaa ggtgttaagc ttattttgct 1380
ttgtaagtaa agaattgtga tattgtgaac agccttttag ctcaaatgtg tgagtcattt 1440
acatatgaca tagcatgaat cactctttac agaaaatgta ggaaacccta gaatacagac 1500
agcaatattt tatattcatg tttatcaag tgagaggact tatattccta catcaagtta 1560

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ctactgagag taaatttatt ttgagtttta tcccgtaagt tctgttttga ttttttttaa 1620
aaaacaaacc ctttttagtca ctttaatcag aatttttaa gttcatgtta cataccaaat 1680
tataatatct aatggagcaa tttgtctttt gctatatctt ccaagattat ctcttaagac 1740
catatgcccc ctgttttaat gtttcttaca tcttgttttt actcatttct gactggacaa 1800
agttcttcca aacaattctg agaaacaaaa acacacacgc agaattaaca attcttttcc 1860
ctgtgcttct tatgtaagaa tcctcctgtg gcctctgctt gtacagaact gggaaacaac 1920
acttggttag tctcttttaa gttacaaaaa gccaatgat gtttcttatt cttttttaa 1980
tttaaattt ttgttataaa tactcacagg ataccttatt tccctagcta tcctctcctg 2040
acttaatgtt ttttaaacc accaatataa atttaattaa agatatatgt tgt 2093

```

<210> 38

<211> 434

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (325)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (403)

<223> n equals a,t,g, or c

<400> 38

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gggcttatag ataaatactt gctttttttc tataacctgt agacttattt ccttttgatta 60
taatgctatt gacactttga taactgtttc tctaaaacct tacaagaaaa actaagcttc 120
tctaaacttg tattcattat gggagaatgc cattcttatg tctggttata tctgcattag 180
gttattgatg atgctagtaa caatgaactt tatgttactg cagctcacaa atgctttttt 240
acatctgcaa gaaattaact agtcatcaaa tgcttagtag cacagaaatt ctcaagtggg 300
tgcggggaaa tattgatcyg caggnrtaaa ttcttcctta aaaataaggg targcaaatg 360
gcmtwtttaa aaaatgggrg gatwtttggg atggtaatgg tgnggggtta ctaaagggtt 420
ttagcccca tagg 434

```

<210> 39

<211> 1078

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (36)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (877)

<223> n equals a,t,g, or c

<400> 39

aggaagtaat tgagagtgtt ggcaacaagg ctgaantata gagaagttgt aggattaact 60
ttttcgccca aagcagcttc acccacgttt tattcccatc gagggagkga gaatgggtgc 120
cgctgagtgg gcgggggagt ggtccctgaa agaggtggag tgctacagcc cctccccgtt 180
ggctctcgct gtttgtccgt tggtggttta tactaatttg acaacagccg cctgttgagt 240
ctcctccaga tcgcagctga aggatctgtt gagcgcttca ggaaaggcgg tgagatccsg 300
taccgcagca gagcactctc agctctgggt cttgcaggcg cagggtccc ccatgccagc 360
agaaagattt cctctggtga agaggaccgt cgaatctgtc ctctcaaga cacctcttgt 420
acagaattta ttcgaatgcc acggccaagg tcttccttga aaaatgttaa ccgatgtgtg 480
ctttttgtct tttgtcatcc tttctttagg acaggcgaca ctaacagggtg aagatctcgg 540
gagaccatga ctaagaaaag aattgctgtg attgggggag gagtgcggcg gctctcttcc 600
atcaagtgtc gcgtagaaga aggcttggga acctgtctgc tttgaaagga ctgatgacat 660
cggaagggtc ctggaggttc caggaaaatc ctgaagaagg aagggtccagt atttacaat 720
cagtgatcat caatacttct aaagagatga tgtgcttcak tgactatcca atcccagatc 780
attatcccaa cttcatgcat aatgccccag gtccctggrg tatttcagga tgtatgcca 840
agaatttgac cttctaaagt atattcgatt taagacnact gtgtgcagtg tgaagaagca 900
gcctgatttt gccacttcag gccaatggga agtggtcact gaatctgaag ggaaaaagga 960
gatgaatgtc tttgatggag tcatggtttg cactggccat cacaccaatg ctcatctacc 1020
tctggaaaagc ttccctggtg agcagcttac caggaaggaa gacccttgac tccacgcc 1078

<210> 40

<211> 1976

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1058)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1919)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1934)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1957)

<223> n equals a,t,g, or c

<400> 40

ggcgtaagac cggagggacg cggcggttagc ggcggccgtt gcgattgatt gcgctggttg 60
cctgcggcgt ccacttcctt ggccgccctt gctacactgg ctgattgttg tgcagccggc 120
gccatgtctg tgagcgagat cttcgtggag ctgcagggct ttttggctgc cgagcaggac 180
atccgagagg aaatcagaaa agttgtacag agtttagaac aaacagctcg agagatttta 240
actctactgc aaggggtcca tcaggggtgt gggtttcagg acattccaaa gaggtgtttg 300
aaagctcgag aacatttttg tacagtaaaa acacatctaa catctttgaa gaccaaattt 360

cctgctgaac agtattacag atttcatgag cactggaggt ttgtgttgca gcgcttggtc 420
ttcttggcag catttggtgt gtatttggaa acagaaacac tagtgactcg agaagcagtt 480
acagaaattc ttggcattga gccagatcgg gagaaaggat ttcactctgga tgtagaagat 540
tatctctcag gagttctaata tcttgccagt gaactgtcga ggctgtctgt caacagcgtg 600
actgctggag actactcccg acccctccac atctccacct tcatcaatga gctggattcc 660
ggttttcgc ttctcaacct gaaaaatgac tccctgagga agcgctacga cggattgaaa 720
tatgacgtga agaaagtaga ggaagtgggtc tatgatctct ccatccgggg ctttaataag 780
gagacggcag cagcttgtgt tgaaaaatag gaggtctctc ttgctcctgg ccttgctgac 840
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gttgctaaac actgcgcttt attttcttaa ccagttgtgg tgtgagtatc agaattgaaa 960
cacttttttg ggggtaaaaa atatagcctt tacatggaca gaattttttt tgttgtttca 1020
gtgaatatgc ctgtaattca gtgtatttca gttccgtnca gaaagtgtaa atgttagttt 1080
cttggtaaaag tccttttctt gcttaccttg actggtgatg tactgattga gaagttcatt 1140
gtctcgtttg tgattcttcc agatgtgatg cttgatattt tctatatgag agttagccat 1200
ccacaccag gcatagctga tacagtataa aaatagataa ttaaaaagat ggttgccaag 1260
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ggatttagta acatcatttt gttttccacc aggcaggag tagggcttag tgttttaaaa 1500
cacctctgct ttctgatgtt gccttaatat tctgctattg cagcaattaa aaattgtctt 1560
catgtacatt tggaaactaac acgtgatgtg atatatctt aaactatgaa acctttttcc 1620
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aaaatcctga ctattatgtt gttagagaaa aatgctttgc tttgtctgga agaaagataa 1740
aatagtgaat tataaataag tcaggccggg cgtgggtggcy cacacygtga atcccagcac 1800
actgggaggc cgaggcaggg ggactgctg agctcaggag ttcgagacca gcctgggcaa 1860
caaagtgagg actccatctc tatatgaaaa acaaaaacca cggaaaggca cacacaaant 1920
aaatccagtg gggntttggt aaatgtgttt tagagtnagg aaatttccag gttgtt 1976

<210> 41

<211> 2310

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (681)

<223> n equals a,t,g, or c

<400> 41

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acagaaactc tctgctatgt tatgccatca tccagtgcga gatgtgctca gtttcctcga 120
gcccaagaca aagttcatta ctacataaaa ctgaaggact taagagatca gttgaaaggc 180
attgaacgaa atatggacgt tcaagagggt caatatacat ttgacctaca gcttgcccar 240
gaggatgcaa agaagatggc tgtaaggaa gaaaaatatg atccaggtta tgaggcagca 300
tatggtgggt cttacggaga aaatccatgc agcagtgaac cttgtggctt ctcttcaaat 360
gggctaattg agagcgtgga gttaagagga gaatcagctt tcagtggcat tcctaattggg 420
cagtggatga cccagtcatt tacagaccaa attccttctt ttagtaatca ctgtggaaca 480
caagaacagg aagaagaaa ccatgcttaa gaatgggtgt tctcagctct gcttaaatgc 540
tgcagtttta atgcagttgt caacaagtag aacctcagtt tgctaactga agtggtttat 600
tagtatttta ctctagtggg gtaattgtaa tgtagaacag ttgtgtggta gtgtgaaccg 660
tatgaaccta agtagtttgg naagaaaaag taggggtttt gtatactagc ttttgtattt 720

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gaattaatta tcattccagc tttttatata ctatatattca tttatgaagg aaattgattt 780
tcttttgggg agtcactttt aatctgtaat tttaaaatac aagtcgtaat atttatagtt 840
gattcttaac tgtgcataaa cctagatata ccattatccc ttttatacct aagaagggca 900
tgctaataat taccactgtc aaagaggcaa aggtgttgat ttttgtatat gaagttaagc 960
ctcagtgagg tctcatttgt tagtttttag tggtaactaa gggtaaaactc agggttccct 1020
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gtaaaaactg gcccttacct gacagagccc tggcttttga cctgcttcag ccctgtgtgt 1140
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tgctgtttgt tactataaat taaatgaacc tcatggaaaag gttgaggtgt ataccttgt 1560
gattttctaa tgagttttcc atggtgctac aaataatcca gactaccagg tctggtagat 1620
attaaagctg ggtactaaga aatgttattt gcatcctctc agttactcct gaataattctg 1680
atttcatacg taccagggga gcatgctgtt ttgtcaatca atataaaaata tttatgaggt 1740
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tggaagcttt gtgcgggtgc tttgaagtgc cttgcatcag ggattaggag caattaaatt 1980
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atccactaga gatgggtttg aggattttcc aagcgtgtaa taatgatgtt tttcctaaca 2160
tgacagatga gtagtaaatg ttgatatac ctatacatga cagtgtgaga ctttttcatt 2220
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tattaagaat tgtaaaaaaa aaaaaaaaaa 2310

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<210> 42

<211> 406

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (8)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (45)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (46)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (350)

<223> n equals a,t,g, or c

<400> 42

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tcacagttct gggaggtgat ctctgatgaa catgcyatcg actccgctgg cacctaccac 120
ggggacagcc acctgcagct ggagcgcacg aacgtgtacy acmacgaggc cagcgggtggc 180
aggtacgtgc cccgcgctgt gctcgtggat ctggagccgg gcaccatgga ctctgtgcgc 240
tcggggcyct tcgggcaggt cytcaggcca gacaaettca tcttcggtsa gctgygggcy 300
arsactgggg tgccgctcct tagccagggc agctcaaaat ccaggaacgn tccaaggtaa 360
tcctgtggga actgtggcgc agggccctga acaacctcct atccgt 406
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<210> 43

<211> 627

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (597)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (614)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (617)

<223> n equals a,t,g, or c

<400> 43

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ccataggaaa tatggtcctc catactcctc agacaacagc cttccgaaag caaacctgtc 120
cctacctgca gatgattaac catctatgaa ccggctgggt aagcaacaag tgccatcttt 180
catggagctg agccttaaag atcctccagt cctaaagctg acgggaagaa ggtaggtggg 240
agcagcgtg aggttttttg aacgtcctca agtgtgtgta caccgataaa ctcatctttg 300
gaaaaggaac ccgtgtgact gtggracca gaagtcagcc tcataccaaa ccatccgttt 360
ttgtcatgaa aaatggraca aatgtcgctt gtctggtgaa ggattctacc ccaaggrtat 420
aagaataaat ctctgtgcat ccaagaagrt aacagagttt gatcckgcwa ttgtcatctc 480
ycccagtggt aagtacaatg ctgtcaactt gggtaaatat gaagattcaa attcagtgc 540
atgttcagtt caacacgaca ataaaactgt gcactccact gactttggaa gtgaagncag 600
attctacaga tccngtnaaa ccaaggg 627
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<210> 44

<211> 745

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (411)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (731)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (743)
<223> n equals a,t,g, or c

<400> 44
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ccgccgcgcc ccgccatgcc gctctactcc gttactgtaa aatggggaaa ggagaaattt 180
gaaggtgtag aattgaatac agatgaacct ccaatggtat tcaaggctca gctgtttgcg 240
ttgactggag tccagcctgc cagacagaaa gttatggtga aaggaggaac gctaaaggat 300
gatgattggg gaaacatcaa aataaaaaat ggaatgactc tactaatgat ggggtcagca 360
gatgctcttc cagaagaacc ctccagccaaa actgtcttcg tagaagacat ngacagaaga 420
acagtttagca tctgctatgg agttaccatg tggattgaca aaccttggtgta acacttggtta 480
catgaatgcc acagttcagt gtattcgttc tgtgcctgaa ctcaaagatg cccttaaaag 540
gtatgcaggt gccttgagag cttcagggga aatggcttca gcgcagtata ttactgcagc 600
ccttagagat ttgtttgatt ccatggataa aacttcttcc agtattccac ctattattct 660
actgcagttt tgcacakggc tttccacagt ttgccrgaa aggtggaaca aggacagtat 720
cttcaacagg ntgctaattg aangt 745

<210> 45
<211> 467
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (25)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (461)
<223> n equals a,t,g, or c

<400> 45
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tactgagagg tctgccatgg cctctcttgg cctccaactt gtgggctaca tcctaggcct 120
tctggggctt ttgggcacac tgggtgccat gctgtcccc agctggaaaa caagttctta 180
tgtcgttgcc agcattgtga cagcagttgg cttctccaag ggcctctgga tggaatgtgc 240
cacacacagc acaggcatca cccagtgtga catctayagc acccttcttg gcctgcccgc 300
tgacatccag gctgcccagg ccatgatggt gacatccagt gcaatctcct ycctggcctg 360
cattatctct gtgggtgggca tgagatgcac agtcttctgc caggaatccc gagccaaaag 420

cagagtggcg gtagcaggtg gagtcttttt catccttgga ngcctcc

467

<210> 46

<211> 722

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2)

<223> n equals a,t,g, or c

<400> 46

nnccctctag tcctgggtcg cgccctgcc catgggtct caggccaggt ctctgctggc 60
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 ggatccattg cccctgagct cccagagtca cccctccacc tccgcagcca gtgaagtgtg 180
 ttgtgctgc tgaagtgatc acccccgc cccagccctg catcaggcca caggctcttg 240
 ctttctcctt atcaccattt gctgttatca cggcacacag cagggaatcc caggccccc 300
 cgccaagtgg ttaccaagt caccactcct gacccaaaaa tcaggcatgg cattaaaacg 360
 ttgcaaatc ctttactgtt atcccccca ccaccaggac catgtagggg gcagtcttta 420
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 ggacttcagg ctggatccac cactgggctc tccctcccc agcctggagc acgggagggg 540
 aggtgacggc tggtagctga tggatgggta gtgggctgag aagaggggac taggaagggc 600
 tattccaggc tcagccctgc tcctgcagct ttgccgctga gtgtaggaaa aacaggcatg 660
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 ca 722

<210> 47

<211> 1002

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (685)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (898)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (905)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (924)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (957)
<223> n equals a,t,g, or c

<400> 47
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ccaggtccct ctgctcccc caccaccagg agccccacct tcaccagccc cagcccgtt 180
cactgcccgg ggtgggagag tcttcaactcc cagagggtgc catctcgccg gggccgagga 240
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cccaagaaac ctcccacagg ccctttgccca ccaagtaagg agcctttgaa agagaagttg 360
atcccagggc ctctgtcccc tgtggcgcg cggaggcagca atggaggtag caatgtgggc 420
atggaagatg gggagcgacc ccgaaggagg cgacatggga gggctcagca gcaggataaa 480
ccgcctcggt tccggaggct gaagcaggaa cgggagaatg ccgcaagggg tctgagggca 540
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cagtggcccc agcacctcgc cgggcagctg ccaagtctcc tgatctgtca aaccagaact 660
cagaccaagc caatgaggaa tgggnagact gcacagaga gcagtgactt caccagttag 720
cgccgagggg acaaagaggc acccccacca gtactgctga caccgaaggc tgtgggaact 780
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agccgttggg gttcttgaag aaggaccggg ccagacgagg ga 1002

<210> 48
<211> 2119
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2093)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2103)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2114)
<223> n equals a,t,g, or c

<400> 48

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 tgtcctgata gttttctttc ccttttctct ggtggcctgt tgtggtgcaa gagctgatgg 180
 cttttgatct tgccccattc aggttgggga gtgaagtgtg aggacccttt tccccgctt 240
 gctgtgaaag cacagattca ttgactacag tacactgttg ttcagaaaag aaggctgcaa 300
 atgacttctg agactttatg tcttttcttc cagaccaaga ccgtagaagg agtcacatct 360
 agccggtcta gccaaagtac aggtgtatat agttcagggc acttgattta gatttgagg 420
 ggctggggtg ggcagagagc aagaggcgag taaagagaat ggtggtttca gagatctctc 480
 ttcccaaagt tgtaaatatt ctataccaga taagtttaaa taagaaattt aattgctgct 540
 taatttttga ttatgtactt tatctgtata gcaggctttg tcgtcagaag tttttatata 600
 gatttaaatt gctgctcttt agcascaaac aggagcaaaa tgtaaaattt ttgaacttac 660
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 ttgcatcttt taaagtattt ttttaagggt tcttggcatt taccctagtt gtccgtgttt 1920
 ggcaatgtgc tgttaaagta atagactttt aatctttatg tattttttgt tttctctgga 1980
 gtacttgagc agatgttata gtggtttctt ttaggaaaaa ctgtcattaa aaaagttata 2040
 gccttgcaaa taacccaaaa aaaaaaaaaa aaaaaccgg gggggggccc ggnaccctaat 2100
 tcncccaaaa gggnggcgg 2119

<210> 49

<211> 494

<212> DNA

<213> Homo sapiens

<400> 49

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 gatcaaagaa accaaagaca gaagatgtag gatgcaggag caatagtgag cagtcacccc 180
 ataatagact ggattcttct gtttctataa aggaacctca gaagctctta cctcaccttc 240
 aagccttttc cttaccctga gagcctcctt taattgtctc ttctttttca ggccaagagg 300
 cccagacaga gttgccccag gcccgatca gctgcccaga aggcaccaat gcctwtcgtt 360
 cctaywgyta ytactttaat ggaagaccgt ggagacctgg gttgatgcag atgtgagtga 420
 ggagagcatk tggggaggga gattcatgaa gggaggggag ttgccatttt ccatgtgttc 480

aattggttgc aatg

494

<210> 50

<211> 1342

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (99)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (381)

<223> n equals a,t,g, or c

<400> 50

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cattttttaat tcacgtgctt tgtgttcagt tttgtggtct gagagatgta ccaattgtca 180
aattaccgtg taccacctaa tgtttatagg agaaagcaaa atacatcagc ttggtagtta 240
acacatcaaa tatttcttgc tgcttctagg agaacttttt tgggtgtgtgt tggaatggct 300
gagcaaatat taaaattgtt aatatgcagc catatatgga aggttcctgt ggggttgttt 360
tttcgtgttt tttttttttt nggtgkggga ttatgtgcct cccattcact agaaaatgag 420
aaaattgtct ggggtccaaa atattgacat tgaatggatc aatacacaca cacagacata 480
tatatatata tgcacacata tataggcagt tgcagtctag catgggtatt tttataacaa 540
tataactgag ttatattgga attataaata ttttcygtca cttaaatttg ttctttgttt 600
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aaaatcgttt ttaatttaaa ctgtgtttta gtgtaaaatt gttaaccttg taagatggat 780
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taaaccacta gttgatgtat ggtatcttta gatatttgcc tgtctgtttg ctcaaaattg 1260
cttctaaaac aataaagatt cttttatttc ttaaggcaaa aaaaaaaaaa aaaaaaaaaa 1320
aaaaaaaaaa aaaagggaga gg                                     1342
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<210> 51

<211> 1527

<212> DNA

<213> Homo sapiens

<400> 51

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gtccccgctc ggcctggcca ggccgcgct atggagtcc tctgggcccc tctcttgggt 120
ctgtgctgca gtctggccgc tgctgatcgc cacaccgtct tctggaacag ttcaaatccc 180
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aagttccgga atgaggacta caccatacat gtgcagctga atgactacgt ggacatcatc 240
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ctggtggagc atgaggagta ccagctgtgc cagccccagt ccaaggacca agtccgctgg 360
cagtgc aacc ggcccagtg ccaagcatggc ccggagaagc tgtctgagaa gttccagcgc 420
ttcacacctt tcaccctggg caaggagtgc aaagaaggac acagctacta ctacatctcc 480
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aaaaaaaaa aaaaaaaaaa aaaaaaa

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1527

<210> 52

<211> 630

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (556)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (628)

<223> n equals a,t,g, or c

<400> 52

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ggtttttttc tcaccttgac tgcaagatga aactccttgt gctagctgtg ctgctcacag 60
tggccgcgcg cgacagcggc atcagccctc gggccgtgtg gcagttccgc aaaatgatca 120
agtgcgtgat cccggggagt gacccttctt tggaaatacaa caactacggc tgctactgtg 180
gcttgggggg ctcaggcacc cccgtggatg aactggacaa gtgctgccag acacatgaca 240
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cccacaccta ttcatactcg tgctctggct cggcaatcac ctgtagcagc aaaaacaaag 360
agtgtgaggc cttcatttgc aactgcgacc gcaacgctgc catctgcttt tcaaaagctc 420
catataacaa ggcacacaag aacctggaca ccaagaagta ttgtcagakt tgaatatcac 480
ctctcaaaag catcacctct atctgcctca tctcacactg tactctccaa taaagcacct 540
tgttgaaaag cmaaaanaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600
aaaaaaaaa aaaagggggg ggggggggnc

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630

<210> 53
<211> 575
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (575)
<223> n equals a,t,g, or c

<400> 53
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aagtttggat ttttgcgatt gtccatagag aagcaggaca cacttttgaa gcttctcatt 180
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ttctcctcct tcamcamcat cgtcacgtac caccttacca aagagctcaa ggatgcaggg 540
gctgggcttc ttgctgctgc catgattgct gtagn 575

<210> 54
<211> 2934
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2767)
<223> n equals a,t,g, or c

<400> 54
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gggggctgaa gagcgccgcg ccctctcgtc ccactttcca ggtgtgtgat cctgtaaaat 120
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gatgtcaata agtctgcttc agatgaccaa tctgatcaga aaactacacc aaagaaaaaa 960
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gactggaagt taaaaaatgt acaagtcctt tcagtgtatg ggaattgat tttttttaa 2640
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aacaatgacc tatttatgat cttaaatctt ttttaaaaa atgtttgtt tctgtgtgtg 2760
gtttttngta tttaaatccg aatgtatgat gtggcagtaa caggtttaact tatgtaattt 2820
cttttagtaca tagggcttag gtttatactc ttggtttcca ctcacactaa tgtcacatgg 2880
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<210> 55

<211> 575

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<400> 55

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ggtaangcta tttggtttta ckascargct ctggaatatt tagcagtcatt tttcactggc 60
acaagagcct ttgtatgtt attcaattta aactttttaa ccaaaaattt tatggtccag 120
tgtctttggc aaaaagatgc tggaggggat gtaacataca attaatatgt ggttatatat 180
atatataaaa agacacaaat tgccatgtta tggttctgcc ttgaaacagc acaatgaagt 240
gtatcagtat attctgtgat tatgaaactt atatgtgtg ttgtttgtg tcttctgttg 300
cctgtccttt ggccagatg tgggccagtt aaatgcagtt atcatctcat taaatacaga 360
tgcagataaa atatcttttag tgctgcaaca ttttacctaa ctttttgtat gttttcatga 420

```

ctgtgtgttta ttttccaaag ctgttcctac ctcacatga ggctttatgg attgttatgt 480
 attataaatg ttctatatga gacagactac tgtgtttctt ctcatttatt aaaagttaag 540
 tagaaaaata aactaatttt aatatctaaa aaaaa 575

<210> 56

<211> 1140

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (563)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1115)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1119)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1135)

<223> n equals a,t,g, or c

<400> 56

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 actgatatcc tgttccggtg ttctgcggg taaactatga gctgaagatg ttgatcatga 120
 tggtaggctt ggtgggctac aacaccatcc tactccacac ccacgcccac gtcctgggga 180
 ctacagccag gtcttatttg agagaccagg catttggaag gacctgaaga ccatgggctc 240
 tgtgtctctc tctatatctt tcatcacact gcttggtctg ggtagacaga atgaatatta 300
 ctgtaggtta gacttcttat ggaagaacaa attcaaaaaa gagcgggagg agatagagac 360
 catggagaac ctgaaccgag tgctgctgga gaacgtgctt cccgcgcacg tggctgagca 420
 cttcctggcc aggagcctga agaagagga gctataccac cagtcctatg actgcgtctg 480
 cgtcatgttt gcctccattc cggatttcaa agaattttat acagaatccg acgtgaacaa 540
 ggagggcctg gaatgccttc ggntcctgaa cgagatcatc gctgactttg atgatcttct 600
 ttccaagcca aaattcagtg gaggtgaaaa gattaagacc attggcagca catacatggc 660
 agcaacaggt ctgagcgctg tgcccagcca ggagcactcc caggagcccg agcggcagta 720
 catgcacatt ggcaccatgg tggagtttgc ttttgccctg gtagggaagc tggatgccat 780
 caacaagcac tccttcaacg acttcaaat gcgagtggtt attaaccatg gacctgtgat 840
 agctggtgtg attggagctc agaagccaca atatgatatc tggggcaaca ctgtcaatgt 900
 ggccagtagg atggacagca ccggagtcct ggacaaaata cagggttaccg aggagacgag 960
 cctcgtcctg cagaccctcg gatacacgtg cacctgtcga ggaataatcc aacgtgaaag 1020
 ggaaaggggg acctgaaaga cgtactttgt taaacacaga aatgttcaag gttccctttt 1080
 ccagagcaa cgtgggcatt cctgaaagag ttcantctnc atttttgggc caagnaagac 1140

<210> 57

<211> 255
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (251)
<223> n equals a,t,g, or c

<400> 57
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gggcatcagg tgctccgaat ctctgtagcc gatgaggccc aggtacagaa ggtgaaggag 120
ctggaggacc tggagcacct gcagctggac ttctggcggg gscctgcca ccttggtcc 180
cccatcgacg tccgagtgcc cttycccagc atccaggcgg tcaagatctt tctggagttc 240
cacggcatca nttat 255

<210> 58
<211> 1254
<212> DNA
<213> Homo sapiens

<400> 58
ggtcacgagg gcagcatgcg ggggttgctg gtgttgagtg tcctgttggg ggctgtcttt 60
ggcaaggagg acttttgtgg gcacaggtg ctccgaatct ctgtagccga tgaggcccag 120
gtacagaagg tgaaggagct ggaggacctg gagcacctgc agctggactt ctggcggggs 180
cctgcccacc ctggctcccc catcgacgtc cgagtgcctt tccccagcat ccaggcggtc 240
aagatctttc tggagtccca cggcatcagc tatgagacca tgatcgagga cgtgcagtcg 300
ctgctggacg aggagcagga gcagatgttc gccttccggg cccgggcgcg ctccaccgac 360
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gtggcggaga acccgacct tgtcagcaag atccagattg gcaacaccta tgaagggcgt 480
cccatttacg tgctgaagtt cagcacgggg ggcagtaagc gtccagccat ctggatcgac 540
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ttcctggaga tcgtcaccaa ccctgatggc tttgccttca cgcacagcac gaatcgcatg 720
tggcgcaaga ctcggtccca cacagcaggc tcccctctgta ttggcgtgga ccccaacagg 780
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atcatcccca cagccaatta ggggtgattca aggtgtctaa ttctagatcg cgaa 1254

<210> 59
<211> 1190
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature

<222> (1122)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1172)

<223> n equals a,t,g, or c

<400> 59

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agggccgccc tccagagccg ccatcttgtg ggagcaaaac caacgcctgg ctccggagcag 60
cagcctctga ggtgtccctg gccagtgtcc ttccacctgt ccacaagcat ggggaacatc 120
ttcgccaacc tcttcaaggc cctttttggc aaaaaagaaa tgcgcctcct catggtgggc 180
ctggatgctg caggaagac cagcatcctc tacaagctta agctgggtga gatcgtgacc 240
accattccca ccataggctt caacgtggaa accgtggagt acaagaacat cagcttcact 300
gtgtgggacg tgggtggcca ggacaagatc cggccctgtg ggcgccacta cttccagaac 360
acacaaggcc tgatcttcgt ggtggacagc aatgacagag agcgtgtgaa cgaggcccgt 420
gaggagctca tgaggatgct ggccgaggac gagctccggg atgctgtcct cctggtgttc 480
gccacaagc aggacctccc caacgccatg aatgcggccg agatcacaga caagctgggg 540
ctgcactcac tacgccacag gaactggtac attcaggcca cctgcgccac cagcggcgac 600
gggctctatg aaggactgga ctggctgtcc aatcagctcc ggaaccagaa gtgaacgcga 660
ccccctccc tctcactcct cttgccctct gctttactct catgtggcaa acgtgcggct 720
cgtggtgtga gtgccagaag ctgcctccgt ggttttgtca ccgtgtgcat cgcaccgtgc 780
tgtaaattgt gcagacgcag cctgcggcca ggctttttat ttaatgtaaa tagttttgt 840
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aagaaaaatc aactcactgt tcagtgtgta gaggggatgt aggcccatgg gcacctggcc 960
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ccaatcgga acattgaaca cacagaaggg gaccgcctag cnagatttgc agtacggcct 1140
ggtgcatcgc cagccagtgt tcctcggaat tnatgtgtgt ggcagacttg 1190
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<210> 60

<211> 580

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (530)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (575)

<223> n equals a,t,g, or c

<400> 60

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attcggcaca ggcgcggacc ggaagtctaa gtggaatccc ggttggtctg gggcgcaggc 60
ttccaacttc gtactctggc ctctgcgtct cggctcgtcg gttgggtacc cgaaccacgc 120
tactgtgctg tgaagagaag atggatgggg actcctcgcc gtcgctgcgc cgccggcctt 180
ccctgggcgg acgtacacct ttgcgaacgt cagtgaggac ccaggggccc tccttggaat 240
agctcttatt tctcaagcgc tgcagcgtga agctcgtctt gcgggtccga gaggcctgcg 300
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```

atctgaagac tgaaaactgg gaagagacgc tctaccctgt gtcctcgcgc ggcttcgata 360
ggagccgcag tgcctgggat tttctcaaac tttgtccaa acttcagctg tgggagtgga 420
ggaacaaaca ggcctctccc agaattgtga aagagatcgc cctgggtgat gaaacaaaaa 480
caaatgcact tgacttcmac gccttgccctg gcgttgtcac gcgggggttn aatgtatgtg 540
gccacatttt aaattccaaa gtattttctt ctaangggct 580

```

<210> 61

<211> 453

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (383)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (403)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (418)

<223> n equals a,t,g, or c

<400> 61

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ttggctcaca ttcattgtctt gtttttgtaa ctggtttgaa gactaaaagg cacgggttca 60
aataagattg gtctcttttg ttggagacta tttctgggtt cattcagttg ttcaagaaac 120
attagttaag cacctactgt tgctagacac tatgctagat actgaggata atgaaggtaa 180
gattgatata gtccctgccc ttatggagct tatagtctca tgtggtctta gtgaacaaag 240
tctcaatttg cttttatact agaaataata aagaaagctg ccttgctgta ttcgatcagt 300
taaaatcagc aatttgtgct tttgtatcag taaaacattt agttctcacc ttttgaaaat 360
gccaaccacg gaagggatta canccccccc attttgggcg ganaagggtt ccgttcgnga 420
gacattttcc aattttgggg gacttcactt tcc 453

```

<210> 62

<211> 2593

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (20)

<223> n equals a,t,g, or c

<400> 62

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cccttgacat ggaaacatn agaacctgag ctgctgttaa tcacctcaa tcagccgggt 60
caaccagccc cattctggcc gcggctcagt ccttgcatcg ggaagctacc aagtggctta 120
gtaagggcaa tgacatcatt gcagcagcca agcgcagggc tctgctgatg gctgagatgt 180
ctcggttggt aagagggggc agtggtagca agcgggcact cattcagttg gccaggaca 240

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```

tcgccaaggc ctcagatgag gtgactcggg tggccaagga gggtgccaag cagtgcacag 300
ataaacggat tagaaccaac ctcttacagg tatgtgagcg aatcccaacc ataagcaccc 360
agctcaaaat cctgtccaca gtgaaggcca ccatgctggg ccggaccaac atcagtgatg 420
aggagtctga gcaggccaca gagatgctgg ttcacaatgc ccagaacctc atgcagtctg 480
tgaaggagac tgtgcgggaa gctgaagctg cttcaatcaa aattcgaaca gatgctggat 540
ttacactgcg ctgggttaga aagactccct ggtaccagta ggcacctggc tgagcctggc 600
tggcacagaa acctctacta aaaagaagga aaatgatctg agtcccagga gctgcccaga 660
gttgctggga gctgaaaaat cacatcctgg cctggcacat cagaaaggaa tgggggcctc 720
ttcaaattag aagacattta tactcttttt tcatggacac tttgaaatgt gtttctgtat 780
aaagcctgta ttctcaaaaca cagttacact tgtgcacct ctatcccaat aggcagactg 840
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gaatcaatgg gaaatactac tcctgtaatt cctacctccc tgcaaccaac tacaaccaag 1860
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tccagtgggt tgagacactg gtttacctt tatgccgat gtgcttttct ccaatatcag 2400
tgctcgagac acagtgaagc aaattaaaaa aaaaaaaaaa aaaaaatccc tgaatgatga 2460
ttagagacat caccgctaaa aaactacatt tataagctag gatttggtat atgcaaatat 2520
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aaaaaaaaactc gta 2593

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<210> 63

<211> 1195

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (80)

<223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (83)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (115)
 <223> n equals a,t,g, or c

<400> 63
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 tagtgaatat ttgttattn atnkkttgcc tcattcttta tatagtaatg gaaancataa 120
 gtctaggagt tagaaatgaa ttttttagac cttagtataa ccatttaacc ataaaatgga 180
 caactgagaa ttctcccagc tgcctgaaag cgtcgccaac tgtgggtatc ctgcaagctg 240
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 gaaggacgga ctaatgatgt ttctcttgcc cttctctggt gcctccattg ccctcatgga 780
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 ttcatcttcc ttgggatata tggatcctct ctaatgagtg taaaagtgcg caaaacacat 900
 ccttattggt cctgatctct tagtcccata aatgggaaca aatacagctt tctgcttctt 960
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<210> 64
 <211> 392
 <212> DNA
 <213> Homo sapiens

<400> 64
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 cacaatgtcc cagtggggaa actgagggcc agagagggga agggacatgt ccaagggtcac 180
 atggtgatgg gacaccagc gctggggccac tgggtccgtgc ctgacctcca gtgggtctgc 240
 cagccaaggg tgaggaaggc tgtggggagg ggaggtggcc aagtcaggct tccccctcca 300
 cctcgtcctc gctggcacag ccctcgga cagctctgcg ccgggatgcc cgcctctcca 360
 ggtactctgc cttaagcygc tctacttcaa tt 392

<210> 65
 <211> 1290
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (229)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (231)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (233)
 <223> n equals a,t,g, or c

<400> 65
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 cccgagcgcc caccgagca ccatgccgc actcctggag cgcccaagc tttccaacgc 180
 catggccagg gcgtgcacc ggcacattat gatggagcgg gagcgcaang ncnaggagga 240
 agaagaggtg gataagatga tggacagaa gatgaaggaa gaacaggaga gaaggaagaa 300
 aaaggagatg gaagagagaa tgtcattaga ggagaccaag gaacaaattc tgaagttgga 360
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 tttacatgag gaagaaaaac ggaggcgaaa ggaacagagt gacctgacca ccctgacatc 480
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 gagccctgga ggacacaatc gcccaggcac cctcatggca gctgacagag ccaaacaaat 600
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 catgcacccc caggctctgc atccagcccc tggactcctt gcttcccccc agctccctgt 1020
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 ccccttcac caacacagcc agaaccgcg attctaccac aagtgaccat cagattatat 1140
 cttcaacacc acacccccca cccatcgtg ggtgagggtg tccctgtgt gtcccaggcc 1200
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<210> 66
 <211> 716
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (93)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature

<222> (98)

<223> n equals a,t,g, or c

<400> 66

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tgttcctgtg tctgaagcca agggcaggag ggnatgntg agttgccaa ggcccagatc 120
agctgcccag aaggsaccag tgcctaaggs tcccactgct actacttta tgaagagcat 180
gagacctggg tttatgcaga tctctactgc cagaacatga attcaggtaa cctggtgtct 240
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<210> 67

<211> 1126

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (416)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1109)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1113)

<223> n equals a,t,g, or c

<400> 67

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<210> 68

<211> 2139

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2067)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2123)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2138)

<223> n equals a,t,g, or c

<400> 68

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<210> 69

<211> 1341

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (20)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (376)

<223> n equals a,t,g, or c

<400> 69

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accaagcaat gaagaacaaa ttaaaaatct gctacaattg gaggtcaag aacatctcca 180
gcttgatttt tggaatcac ccaccacccc aggggagaca gccacgtcc gagttccctt 240
cgtcaacgtc caggcagtc aagtgttctt ggagtcccag ggaattgcct attccatcat 300
gattgaagac gtgcaggtcc tgttgacaa agagaatgaa gaaatgcttt twaataggag 360
aagagaacgg akggtnaact tcaattttgg ggcctaccat accctggaag agatttcca 420
agaaatggat aacctcgtgg ctgagcacc ttgtctagt agcaaagtga atattggctc 480
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<210> 70

<211> 735

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (628)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (730)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (732)

<223> n equals a,t,g, or c

<400> 70

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 caaagggttg ctctccctg ccaaggtnga ctccgaaaag ccctctttgt tctgccccaa 660
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<210> 71

<211> 2030

<212> DNA

<213> Homo sapiens

<400> 71

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catagacaag gctcccttca cgtgggggat gagatcctag aaatcaatgg cacaaatgtg 480
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<210> 72

<211> 1875

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (339)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (350)

<223> n equals a,t,g, or c

<400> 72

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ctttcaagct ttctaaagtt tccaccaacc tcagatgaaa atgtaactgt gagaagtaaa 180
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<210> 73

<211> 860

<212> DNA

<213> Homo sapiens

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<220>

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<222> (13)

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<220>

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<222> (40)

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<220>
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<220>
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 <222> (857)
 <223> n equals a,t,g, or c

<400> 73
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<210> 74
 <211> 520
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (34)
 <223> n equals a,t,g, or c

<220>
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 <222> (485)
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<220>
 <221> misc feature
 <222> (498)
 <223> n equals a,t,g, or c

<400> 74
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<210> 75
 <211> 863
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (2)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (6)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (772)
 <223> n equals a,t,g, or c

<400> 75
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 tagtccaggt agggcccaga aataggaaaag gctaggattg gataatgctg caaatgcttt 720
 ttttgtgtga gaaactggga gagatgtgat ttctcctttg gggagagaat tntcccaaat 780

ttgatttagg gtgagccttg ggaatagttt tggcaggttt taacatccca aggggtaacc 840
taacgtagtt tgggaaaagg tag 863

<210> 76

<211> 691

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (674)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (681)

<223> n equals a,t,g, or c

<400> 76

aagaaaagaa gatgtagcct cttttccaga ataagagtac tgactaagct gcctgaaagc 60
ttgtcactga ttctttgctt caggagtctc agctagggag ttgaagtgtt tacatcagac 120
tgtcttgtgc aattcttata tttattttac tggttcactt ttttttacct ttatttttagt 180
ctttatatatt ttatttttaa gcattgatgt acttagttgt tgaaaggggtg atgaaactga 240
tatccagata cttgagatcc tggtaattgg tcataaataa ttggcaaaat aacaaattgt 300
gaaaatagaa gccattgctc agcaccgttt ctccatcaat gccgtgaact tgccttactt 360
gagggaaaaat tctttaactt tggaatattg cattgaactc agctatacac ataaaacatt 420
ttctttggta aatcaagatc cagtcagggt ttctcttgaa ttattttgga acaatgccag 480
gatccaaact gattaagtta cagtttaagc acccttcagt attaatatat acggtattat 540
ataacaggtc aacaagtgtc ctttgatgat aaaacttgta atagagcaat aattgtaaat 600
ggttaccata ctgtaagata ttttgataaa aattaactag taatacttgt atttatttga 660
aacactgggg gggngggagt nggggggggg g 691

<210> 77

<211> 325

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (310)

<223> n equals a,t,g, or c

<400> 77

cccacgcgtc cgggcggcca ccgcgctgct ggaggccggc ctggcgcggg tgctcttctta 60
cccgacgctg ctctacaccc tgttcgcgcg gaaggtgccg ggtcgggcgc accgggactg 120
gtaccaccgc atcgacccca ccgtgctgct gggcgcgctg ccgttgcgga kttgacgcgc 180
cactgggtaca ggacgagaac gtgcgcgggg tgatcacatc gaacgargar tacgagacga 240
rgttcctgtg caaytyttca caggtgcaca aatggaatcc agaagaagct gtaagaccat 300
cgccaagatn cggtcataca tccaa 325

<210> 78

<211> 821
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (45)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (54)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (690)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (771)
 <223> n equals a,t,g, or c

<400> 78
 acttagttct agatcgcgat ctagaactac ccacgcgtcc gcggnacgct ggginctctgt 60
 gaattctgaa tgtaaaaac caacactgct tttaatcctc ttttaatgtt ttaatacrag 120
 ctttctgttc tgaaacaagg ctgcataagt agaatgggaa tccttctaaa ggtgggtgtg 180
 aactcaccac aagctgagct ttatagagcc cttgagaaac cctcctgagc actaagcagt 240
 tggggtgctg attttcttgt acttttgaaa aattaagtca ctcccagttt cctgcataag 300
 ttcttgaaca gaatgaaatc acatctccat tcaaaaaatg tctcaagcat ctactgttgt 360
 gtaaggaact tctgattctg attgctgtta cttgaatagg aaatgggttac tcattctgta 420
 taaaagtgtt gcaagagaat gaatttttta ttctgtaatc aaaaagcaat aacttgaaat 480
 tcaactctgta atattatagg kcagaattat acaagtttta ccaaattggt acacttattc 540
 tccaagctgc cagaacctgg tatctgtatc tgtaaaacca aattaacttt tgcttaaattg 600
 ggaagtatac atatatctgt atagatacat tacccttcta catgtttaac atacacacac 660
 ttaaacacat aaatactagt gtgattatan tttggagttt gcaatatagc ataaaggaca 720
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 gaggaatttg tccacaggaa ggtgaggaat tccaatgagc c 821

<210> 79
 <211> 617
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (538)
 <223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (595)

<223> n equals a,t,g, or c

<400> 79

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cttcccaccc cagacgtcac cacagggacc agaattgaaa cgaccttcgg acccgccctt 120
tcagccgtca ccaccatcac aaaagctgac gggaccagca cctacaagca gcaactgcagg 180
acacctcct cctcsagcac ccttgccctac tccccgcggg acgaggagga cagcatgccc 240
cccatcagca ctccccgccg ctccgactcc gccatctctg tccgctccct gcaactcagag 300
tccagcatgt ctctgcgctc cacattctca ctgcccagg aggaggagga gccggagcca 360
ctggtgtttg cggasagccc tcggtgaagc tgtgtgttca gctctgctgc agcgtcttca 420
aagaccccgat gataccacg tstsggcaca cgttctgtag gagatgcgcc ttgaagtcag 480
agaagtgtc cgtggacaac gtcaaaactga ccgtggtggt gaacaacatc gcggtggncg 540
agcagatcgg ggagctcttc atccactgcc ggcagtgccg ggtaacgggc aagcnggaaa 600
gcccccatct ttgaagt                                     617
```

<210> 80

<211> 1189

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1107)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1156)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1167)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1188)

<223> n equals a,t,g, or c

<400> 80

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gtatcaaagg gaaagagtat ttctccttaa ataaaattac aaataagaaa tgtatgtttt 120
actcttactc ataaaaggta ttgtagaata caaaagggtt ttcaaactgg ttttgtcttt 180
gattggcttt tataatccac acttcaaaga agaaatgcat ttaactttta ataacttagt 240
caaaaagtat aatgttgcct tgccttgcac aacctttaac tattgcaaag gatgttttgt 300
ccttccccct tgtccagtat ttccaaatg gtcaacagtt taaacattta agcttgcact 360
gagaaaacct gccacatttc agcagttttg ttttgctttt ggtggagagc acctgatctc 420
gacttttacag ccaatgtatt tactctaaat tacactttta tagatacaag gtaaagtgtg 480
```

```

gctgggtgaa ggcactcagg agccataaaa tgtggtcaac cacaataaat taaaatgtaa 540
gctaaacaaa gtattcacac ttgcattttt ttaataagga atttaagatc catagtatct 600
ttaatgcttg gaagagacac aaattcaagg tgataaaaaat attaattaga agacacataa 660
catgcctcaa gtatatcaac acttgactcc acaacaagg cataaccatg aaaacaacac 720
tccctttatt ttgggctccc aaaatcaaaa gttagaacta atttatttaa tcacagatat 780
ttagtatact caataatgca ctaacaattt ctttaaaaaa aactaatac tgtacagtat 840
ttctgtgttt tagtttttcc cacagctgtt gaaaatttca gccttgattt gaaacatgac 900
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aagatgaaaa ggtattggca ttggtcntaa tagatgttg catctctggg gtgaggatgc 1140
tgactgagcc tgttcngtgt cttcatncac ccccatgtgt tttcttct 1189

```

<210> 81
 <211> 466
 <212> DNA
 <213> Homo sapiens

```

<400> 81
gcggcggcgg cgcgggcctg cagggcctgc cgggcgcacg tggcggcctc gggcctggga 60
gccgggccgc gtcctctctc ctccggccgc cggccaccgc cgaagtctta gggcgggggg 120
gctcgccccg cgcaggagtc accccaactt tcacggctcc aaaaaatact tcccgagttg 180
ggggaggggg ccaccgagcc acgagcagga gtggcttttg tccctcatcc ttgtttactc 240
ggagaaactt cagaccggac gtgtttagtc agaacagaaa tacatctcag ggccaaaccg 300
ataggaaacg aggtgcctc gcggtggcac cgcaccyccc aaccgggttc cgagcaccgc 360
agctggctgc tgctccctct ttggagcaaa gttttatgca aagagggtgt tttttgaaac 420
tttcggtgca cggtgatatt tttttttaag gtcccataat taggaa 466

```

<210> 82
 <211> 360
 <212> DNA
 <213> Homo sapiens

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<400> 82
atctgggaat caagtaggtt ttggtctgt gcttttataa gtatttcttc tatgtgaaat 60
cactctaagt ttgaatagta gaatttctta tcttttgacc aagatgtgtt acataaactt 120
gggttagcat aaaaaaacia aaatttttta aaccctcatg tgtcttaaag ataatagtag 180
actagaaata ttaagagctg aaccaagagt tttaatgtat ggtaatttga aataatttta 240
atttactgga taattttatt ttaccagtat attacaagt gagttgrctg gaagggtagt 300
ttccaacccc aagctggtaa taccagttcc aaggggccac cattaacagc ttgggccctt 360

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<210> 83
 <211> 2109
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (2066)
 <223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2083)

<223> n equals a,t,g, or c

<400> 83

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agatgtcttt ggggtgggga acctcacctg cccaatctgc aaaggtctat tcaccgccat 60
caacctcggg ctgaagaagg aacccaatgt ggctcgcgtg ggctccgtgg ccatcaagct 120
gtgcaatctg ctgaagatag caccacctgc cgtgtgcaa tccattgtcc acctctttga 180
ggatgacatg gtggaggtgt ggagacgctc agtgctgagc ccatctgagg cctgtggctg 240
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ctgtgccgaa gccgcccccc aaacccccta gccccccagc cccagggtgc cctgtcagcc 360
gcatcctctt cctcactgac ctgcaactggg atcatgacta cctggagggc acggaccctg 420
actgtgcaga cccactgtgc tgccgcccgg gttctggcct gccgcccga tcccggccag 480
gtgccggata ctggggcgaa tacagcaagt gtgacctgcc cctgaggacc ctggagagcc 540
tgttgagtgg gctgggcccc gccggccctt ttgatatggt gtactggaca ggagacatcc 600
ccgcacatga tgtctggcac cagactcgtc aggaccaact gcgggcccctg accaccgtca 660
cagcacttgt gaggaagtgc ctggggccag tgccagtgtg ccctgctgtg ggtaaccatg 720
aaagcacacc tgtcaatagc ttcctcccc ccttcattga gggcaaccac tcctcccgt 780
ggctctatga agcgtatggc aaggcttggg agccctggct gcctgccgaa gccctgcgca 840
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cctggcaccc agtgcaacta cctacatcgg ccttaatcct ggttaccgtg tgtaccaa 1260
agatgaaac tactccggga gctctcacgt ggtcctggac catgagacct acatcctgaa 1320
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cctggagctg gtttagctgg atatgggagg gggtttggt gcctgtgcc aggagctaga 1860
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tgggcagaca agacaggagc tgtcgcccca ggctgtgct gccagccag gaaccctgta 1980
ctgctgctgc gacctgatgc tgccagtctg ttaaaataaa gataagagac ttggactcca 2040
raaaaaaaaa aaaaaaaaaa ggcggncgtt cttagaggat ccntcgaggg ggccaagt 2100
taagctggc 2109
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<210> 84

<211> 1535

<212> DNA

<213> Homo sapiens

<400> 84

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cttcatgtta gtcttagaga aacaggaaaa atactgatgg tcaccagcag ttcttcgcaa 60
tcgtacagct gataggaaca cgcaagcaag ctgaaaattt tgcttaccga cttgagctaa 120
```



```

atggtcatag gcgacgattg acttggaag cgactcctcg atctattcat gaaggaattg 180
caacagccat tatgaatagc gactgtctag tctttgacac cagcattgca cagctttttg 240
cagaaaatgg caatttaggc atcaatgtaa ctatttccat gtgttgaaat ggcaatcaaa 300
cattttctgg ccagtgttta aaacttcagt ttcacagaaa ataaggcacc catctgtctg 360
ccaacctaaa actctttcgg taggtggaag ctagacacat gaaggtaaata aaaaagaaaag 420
gctgttaaata acaggaaaca gttgcatgta gtaacactaa tatattttaa aataagtcaa 480
cagtaaacca ctgaaaaaat atatgtatat acaccaaga tgggcatctt ttgtattaa 540
aaaggaagca ttgtaaaata attctgagtt ttgtgttgt tgtagattga ttgtattgtt 600
gaaaaagttt gtttttgcgt gggagtgtgt gcctgcgtgg gtgtgtgcgt gtttgggttt 660
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taaaaaggca gtttgcaaaa aatgtttttg gtcttttata attctcatta aaagaatatc 1320
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tattttcctg tttcattcca tactttaatt atatagcaga aagctgtgtg ttgtcatttt 1440
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```

<210> 85

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (325)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (334)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (347)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (381)

<223> n equals a,t,g, or c

<400> 85

cggggatcca agcagccccg gggagagggg ggctgcgtct gtatccgggc ccaaggtcac 60
cgcgcgaccg gcagatgcgt gctgcaggcc ccggccacat gagcagcgct acggacgcga 120
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actcggcctg cccagsets tgcttcaccc cactggtggc caaatagccg atgtctaata 240
ccccacacaa gctcatcccc ggcctctggc gattgttggg aattctctcc ctaattcacg 300
cctgaagggtc atggagagtt gctanaactg ggantgccct gggaagngca aaaaaccaag 360
ccgggttgca gcaagacttt nccagtcctg ttttttggg cgtgattcgg ccggaacatg 420
caggtgatag t 431

<210> 86

<211> 1142

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (478)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (565)

<223> n equals a,t,g, or c

<400> 86

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ggctgcattg atgtcgggct ctcagtgatg tctgtaaaga agtcatcaaa atgsatagac 180
cttgacaccg aggagcacat ctaccatctg aagggtcaagt cagaagaagt ctttgatgag 240
tggttatcga aacttcgcca ccacagaatg tatcgtcaga atgaaattgc catgtttcca 300
catgaagtta accacttttt ctcagggtcc accatcacag actcttcac tgggggtgtt 360
gactccattt caagtaggaa gcgtacagtt atatcaaagc agaatttatt tcaaactggg 420
aagcaatgta tcattttctt gtggtggtga gacacgagtt ccattatggt tacagtentt 480
cagaggacat ggaataatgc tccaaagacc tggcgactg tcatgcctac ctggtagaaa 540
tgagccagct cctgcaaagc atggnacgtc ctgcatcgga catactcggg caccagctat 600
caacgccatc caggtcccga aacctttttc tggcccagta agactacact cctccaatcc 660
taatttgtea aactagatt ttggagaaga gaaaaattat tctgatggct ctgaaacctc 720
atcagagttt tctaaaatgc aagaagatct gtgtcatatt gcccataaag tttacttcac 780
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aa 1142

<210> 87

<211> 1797

<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (645)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1793)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1794)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1796)
<223> n equals a,t,g, or c

<400> 87
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gggcgtatct catggcggac atggctcaca tcagcgggct ggtggcggct ggcgtgggtgc 180
cctccccatt tgaacactgc catgtggtga ccaccaccac tcacaagacc ctgcgaggct 240
gccgagctgg catgatcttc tacaggaaaag gagtgaaaag tgtggatccc aagactggca 300
aagagattct gtacaacctg gagtctctta tcaattctgc tgtgttccct ggccctgcagg 360
gaggtcccca caaccacgcc attgctgggg ttgctgtggc actgaagcaa gctatgactc 420
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tggtgggagg gttttgctgt cagtatgctc aagtatggtg tagaaatggc ctctccctc 1500
catcctggga agtcccagtc ccacctggt gtgagaatca accaggcttt cctgtccac 1560
ctgagataac caactccctc ccgtaatcag gaagccaaat gtcaccttcc caaagaaatt 1620
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<210> 88
<211> 381
<212> DNA
<213> Homo sapiens

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acctcaggaa gctgcagctg gagggctggg gcacctgccc cctgtctccc cacacatcat 240
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taaagcagtt tattttctga g 381

<210> 89
<211> 538
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (24)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (53)
<223> n equals a,t,g, or c

<400> 89
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<210> 90
<211> 2121
<212> DNA
<213> Homo sapiens

<400> 90
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ggcaaccacg atggggctgt ccagcaatat atccgaacca ttggaaagtt ggagccatcc 180
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<210> 91

<211> 2974

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2833)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2862)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2938)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2942)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2949)

<223> n equals a,t,g, or c

<400> 91

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<210> 92

<211> 412

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (136)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (229)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (349)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (371)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (383)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (404)

<223> n equals a,t,g, or c

<400> 92

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cgcacggagc ctcgctcggc ctcgggggag ccacgagagg tgggagttgg acccgcagcg 120

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ggccaggagc cctgtncatt ggaggacccg ccaaaaagga agcaaaccct ctttttcttt 180
atccaacccc aaatagctag ggcctagggg gaagactcac atatcgatna aatggtttgt 240
tgcccgtttt attctctggg aaatacaact grtcttacca aaggaaatta acctgtcttt 300
ttggccgtgt ttaatttagg aggccatagg attacctgtt ttcagaggnt ggaaggggac 360
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<210> 93
<211> 1883
<212> DNA
<213> Homo sapiens

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<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (252)
<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (1591)
<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (1819)
<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (1883)
<223> n equals a,t,g, or c

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<400> 93
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tcagcaagac aattgaagaa tatgcagttt gccctgacct gaaagtagac cttggtgttc 600
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attcggtaga agcttatgct acaatgctga gaagcatctt tgatttcagt gactgaaaag 720
aactactttc tgggccaac cgaactgaaga tccgtattga tgctatgcat ggagttgttg 780
gaccgtatgt aaagaagatc ctctgtgaag aactcgggtc ccctgcgaac tcggcagtta 840

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actgcggttcc tctggaggac tttggaggcc accaccctga ccccaacctc acctatgcag 900
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<210> 94

<211> 2311

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (7)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (689)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1657)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2311)

<223> n equals a,t,g, or c

<400> 94

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cagaccctct ccccagaagg acccgagacc cttgttattg cctcgcttag atccaggaca 420
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<210> 95

<211> 514

<212> DNA

<213> Homo sapiens

<400> 95

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gaaggatctg ctacgcgtct tccaggccta ccagctaccc gctgatgact acaccagtct 180
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agaaggtagc tagagrgcc caagccccag ctccatctc cacttattyt gcctgtttcc 420
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tggctgrrca ggmthcttga ctggcacctg gaaa 514

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<210> 96

<211> 465
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (375)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (406)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (417)
<223> n equals a,t,g, or c

<400> 96
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<210> 97
<211> 1459
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (649)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1104)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1418)
<223> n equals a,t,g, or c

<220>
<221> misc feature

<222> (1434)

<223> n equals a,t,g, or c

<400> 97

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agaagcactt cccggacttc agggggcgacc cgcacaggct ggaggacgtc cagcgctacc 180
tgggtccagt cttcgacagg aagagacgga accgcagcaa gccactcttc caccacttca 240
ccaccgccat cgacaccgag aacgtccgct tcgtgttcca tgctgtgaaa gacaccatcc 300
tgcaaggagaa cctgmrggac atcatgctgc agtgagcgag gaagccccgg ggtttgtcgt 360
cgttgagcag cccccacggc tgtcggtcag actcttgggt gtgtgtgtgc tgtgtgtgcc 420
ttgagtgggt ttctcgatc cgtgccctgg aatacctggc tcaggaatgc tgtcagacca 480
gccagccagc gagctctagg caaaaggaca tggaaactgt cacgttagct actgaatcct 540
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<210> 98

<211> 879

<212> DNA

<213> Homo sapiens

<400> 98

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ctcaaaaatg ctacgtctct cccatcctta tcctgtgcct cttactactt ggagttctca 180
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tacacatgag gccctactt ctcaagctgg gaaggccaag agccttctt cagcctttct 480
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cttccctctg gactgtagag gagctaactg tttggaacag aaaactgctg gctgttgatt 660
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cagttctttc tcctcagttt ccaaagtaaa tggggaatcc cagctttctt ttctactagc 780
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<210> 99
<211> 248
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (4)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (9)
<223> n equals a,t,g, or c

<400> 99
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aaacgagatg tggaggtaga agacagtgat atttgaccct gatcctatgt aggtctaggc 180
taatgtgtgt gattgtgtct tagtttttaa caaaaaagtt taaaaagtaa aaaaaaaaaa 240
aagaattc 248

<210> 100
<211> 480
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (414)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (473)
<223> n equals a,t,g, or c

<400> 100
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gttgactgtg ggaaactcgg aaacaagctc acatcttcct gtgggaaacc ttctagcaac 120
aggatgagtc tgcagtggac tgcagttgcc accttcctct atgcggagggt ctttgttggt 180
ttgcttctct gcattccctt catttctcct aaaagatggc agaagatttt caagtcccg 240
ctggtggagt tgttagtgtc ctatggcaac accttctttg tggttctcat tgtcatcctt 300
gtgctgttgg tcatcgatgc cgtgcgcgaa attcggaagt atgatgatgt gacggaaaag 360
gtgaacctcc agaacaatcc cggggccatg gagcacttcc acatgaagct ttnccgtgc 420
ccagaggaat ctctaacatt ggctggsttt tcctgstggt gtcctccggt tanaagcccc 480

<210> 101
<211> 453
<212> DNA

<213> Homo sapiens

<400> 101

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gatagtggag aagccgcaga cgaatggagg agctgaggat gctggaagaa gagaaccagg 60
gtggaggaag tgacatgccc tggagacttg tgggaagtgg gttggaggga ggccaggccg 120
gcagcgggag gccctgggag aaatggagag aggtcagcgg agggctggcc tcagccgcgg 180
ctccttggtg ggtgcctggc ttggcaactg ctagagcagg gaggggggag ggcaggggat 240
tacctaatta gagtgggtta gcttagattg gtagctgctg aaactctcgt tgagtcagga 300
rcgggtaaaa ggtaggtggg gtggggagtg kggccccggg gtggggcctg ggcctctgcg 360
tgcaaacccc agcctccctc ttcttcctca ggctttggag cccctgagtt tgagttcaat 420
aaaaacttta tgtggtaaaa aaaaaactct gcc 453
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<210> 102

<211> 903

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (846)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (875)

<223> n equals a,t,g, or c

<400> 102

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ataacagtta acaggatgca gacatggcag aggtttccta aaaatctcat tatctataac 180
catttctata ttacatttg aaaatctcct ttggagactt agaacctcta aattattgac 240
ttatttttta tataaggatg ctccgatgaa aggtgattac aaaatcatct acattgctgt 300
ctacaaaaca gataatatgg atgtttgatc gcattctcatt gttaactctt tactgatatg 360
tttgtaaata cagaagtga atgtggacat aaaatagtta cgctatttgg ttaatggtac 420
tagacaacat gtaattaatg acattcaaaa atttatggct agtgatata ataaagtaaa 480
atthttcttg cagtaaaata tgccctttat tatagaaggg aggatataag gaaccaacag 540
tttgatgaa aatagctcaa ataatatctt ttattttgat tttaatatth cttattttgg 600
tttattagtg tcttagaaca aaatggcctt atataatgaa gcctagttat gctgggactg 660
ttttgatctc ttttaattgt tctggacaga tagttgggga tgagagccga ataaggtttg 720
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gtcattcctg gtaggaacca agctttatth ttcgagccta gccaatgatc taggagccag 840
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aag 903
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<210> 103

<211> 1788

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature
<222> (63)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (246)
<223> n equals a,t,g, or c

<400> 103
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atngtttgtt ctctttcaga cataatttag taggggacaa gaagtctgtt cttcagttag 120
tacctagag atttactctg gtgactgcct tttgagttat gggtagtaa ggtatggctt 180
taccataacc ttgattcatt cacccttga ttcatcttc gcccccgta ctgtatttcc 240
ttgagnatat atctctgcct aacacttttag taggtgctat agaggatata tgaaaagtat 300
gagatctggt tccatccagt aagacatttt aatagagaag atcaaaatgt tacctggcag 360
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atatttcaac cagagacaca actttctggc agacagacaa attgtacaac accaacaata 480
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ccctctccac ttctgaagta tgatgatgta ttaaggatgg aggagttatt aaaaatgytc 660
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<210> 104
<211> 3319
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2555)
<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3313)

<223> n equals a,t,g, or c

<400> 104

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caaaaggcaa tccgggaaga ctaaggagac aagcgtcaac tgggtgtctg ctgatggcta 240
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caggatctac tgagactctc ctatgggtgag gccaaagaaag ctgcccgtga ctacgagacg 420
gccaagaact acttcaaaaa aggcctgaag gatatgggct atgggaactg gattagcaaa 480
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caggggatct tttttctccc ttttttttct tttttaagcc ataattgggt atactgaaaa 660
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<210> 105

<211> 1986

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1227)

<223> n equals a,t,g, or c

<400> 105

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ctgtatgaca gcctagggtc tttgggtgtg ggacacctat taggcatggt ctcagcattc 180
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agaatggcgg ctgggtgatc tctttgctga attaatgagt tcttaacatg tggaccaaac 1860
tgcctgtgtg agatctgtgt cttaaaactt actggaatgg aaatctatga attattgcaa 1920
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aaaaaa                                     1986

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<210> 106
<211> 591
<212> DNA
<213> Homo sapiens

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<220>
<221> misc feature
<222> (565)
<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (567)
<223> n equals a,t,g, or c

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```

<220>
<221> misc feature
<222> (583)
<223> n equals a,t,g, or c

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<400> 106
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gctgcgggtg ctttttctag aagtgaatgg aaatcttgct cagttggcat ttcaagcagg 180
aatgaaaatg cttgctttta tggcaaagca gcgttaacat ttttcctgtc gtgtagcaga 240
gagtacaaga atcatttcag caaagcagtg actcaccatg agacgttatc tccatggagc 300
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tcatgtcac aatgaaactg ttcattacat caactgatct ctctctctct ctcttctct 420
ctttctcttt ctccataacc ccaaggcaaa atttttttta agaaatgact ttaaaaacta 480
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```

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<210> 107
<211> 153
<212> DNA
<213> Homo sapiens

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```

<220>
<221> misc feature
<222> (144)
<223> n equals a,t,g, or c

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<400> 107
tccccgggc tgccagaatt cggtcagagt gcatccttac ctttggtgcc agctgctgtt 60

```

gctgccccct ttgatgatga tgacaagatc gttgggggct acawctktga ggagaaattc 120
tgtcccccta ccagggtgtcc ttgnaattct ggc 153

<210> 108

<211> 1536

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1482)

<223> n equals a,t,g, or c

<400> 108

aattcggcac gacggaactg ccacgatgct gccactttgg actctttcac tgetgctggg 60
agcagtagca ggaaaagaag tttgctacga aagactcggc tgcttcagt atgactcccc 120
atggctcagga attacggaaa gacccctcca tatattgcct tggctctcaa aagatgtcaa 180
caccgcgttc ctcttatata ctaatgagaa cccaaacaac tttcaagaag ttgccgcaga 240
ttcatcaagc atcagtggtc ccaatttcaa acaaaataga aaaactcgct ttattattca 300
tggtattcata gacaaggag aagaaaactg gctggccaat gtgtgcaaga atctgttcaa 360
ggtggaaagt gtgaactgta tctgtgtgga ctggaaaggt ggctcccgaa ctggatacac 420
acaagcctcg cagaacatca ggatcgtggg agcagaagtg gcatattttg ttgaatttct 480
tcagtcggcg ttcggttact caccttccaa cgtgcatgtc attggccaca gcctgggtgc 540
ccacgctgct ggggaggtcg gaaggagaac caatgggacc attggacgca tcacagggtt 600
ggacccagca gaaccttgct ttcagggcac acctgaatta gtccgattgg accccagcga 660
tgccaaattt gtggatgtaa ttcacacgga tgggtgcccc atagtcccca atttgggggt 720
tggaatgagc caagtcgtgg gccacctaga tttctttcca aatggaggag tggaaatgcc 780
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tcgagacttt gcggcctgta atcacttaag aagctacaaa tattacactg atagcatcgt 900
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tctcaaacca gatagtactc attccaatga atttgactca gatgtggatg ttggggactt 1260
gcagatgggt aaattttattt ggtataacaa tgtgatcaac ccaactttac ctagagtggg 1320
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aaccgtcagg gaggaagttc tgctcaccct cacaccgtgt taggagacta ctgttatttg 1440
accaatgaat tgacttctaa taaaatctag tgggtgatgca anaaaaaaaaa 1500
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaagg 1536

<210> 109

<211> 512

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (29)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (55)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (58)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (60)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (512)
<223> n equals a,t,g, or c

<400> 109
tggaacggtc ccttcgacgc cgcacctgna aacttcaatg ccatgccgcc caagncgnon 60
ggatgacgtg gcacagccaa gaaacagtct gggagaatcg aagttccaac aagtgcccg 120
ggaccctgcc acatatggac agttctatgg aggcgacagc tacatcatc tgtacaacta 180
ccgccatggt ggccgccagg gcagataatc tataactggc aggggtgcca gtctacccag 240
gatgaggtcg ctgcatctgc catcctgact gctcagctgg atgaggagct gggagggtacc 300
cctgtccagg tgagcccagc ccaccscctc tctgggctgc agcctgagcc ttgtccttct 360
cttcaatcat ctgtctgact ctcatccatc cattcgtttg tccatctgtc tgtctgtcca 420
tscatccatc catccatcca tccatccatc catccatcca tssaacagrt attgattcct 480
gggctgactt cgagcttaat atttttttat tn 512

<210> 110
<211> 1455
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (786)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (846)
<223> n equals a,t,g, or c

<400> 110
ggcacgagcc caccagcct gccccaggt ggacatccca gccacctaga ccttcctgtg 60
agtgaaccag ccccttccac tctcagactg gcctattggt gtgggccccg tgaggcagtc 120
ataacacagg gatgaaacct ggctctgsca cttcccaagg tgggtgactt cacttctctg 180
agcctcagtt tcctcttctg agcatgggcc tgaatgagac gtgtgtaaag taccaagcac 240

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agtgggtgagc caatggaaga cacgcagyta gccaccagca gtcacaccca aagatgcctc 300
tgatttgtga ctctgaaaat tcttgcaaag ctgagaaggt gaaattcctc tggctatatt 360
gttgacccaaa ggccctcctc tgtaagagtg aattgcacgc tcaattgaaa ctatcttgag 420
ggactaagggt gtacaatcct ggtgcttatg cagtttgggg ctctaggtag acacgagctg 480
gctttgaaat tgtagattcc tacactcccc tttcttrgag ttctgggtct aagtgaattg 540
actcctatct ctgttgtaga tgttgtagtt tcccttccca ttctcttggg ggccctggaa 600
gcttctaggg acagtgtgca ccctgattat tcccaccact ccatccaact tttctctctc 660
tgtgggtgtc gcaccacaag ctgcctaccc tccaggtgcc tcaatgggtc ggccaccagt 720
tgtgcctcgg cgcctcccg ccacacatcag cagtgtcagg caggcctcca cccaggtgcc 780
acgcanggtg cctcataccc agagagtagc caacattggg actcagacca caggacccag 840
tggggntagg gatgctgtac accaggcccg cgcctcctgc cgtgcaaag ttcctcagca 900
gcacatagca cctatcgggt ccaggagccg gctgtgcaca tcccaggaca ggagcccstr 960
accgcgtcca tgctggctgc ggcgcccctg catgagcaaa agcagatgat tgaagggtgt 1020
ccacacaggg gagcgtctct acccccttat ccatgatgtc cacacccagc tggctggcaa 1080
gatcacgggc atgctgctgg agattgacaa ctcrgagctg ttgctcatgc tggagtctcc 1140
agaatccctc catgccaaga tagacgaggc agtggccgtg ctgcaggcac accaggctat 1200
ggagcagccg aaggcgtaca tgactgaaa ccagaaaagg aaatcctcgc ttccatggct 1260
gccaaaagga cagtgtttct ggctctcagc cctaaggccc tgcaaactct aacttatttc 1320
ccaattagtc tgtatctata cttgggctct gtatgtgaat gaagggtggg caccatcca 1380
gcctattacc ttttgcttg tgattaaaa gtgctgcaaa atcaaaaaaa aaaaaaaaaa 1440
aaaaaaaaaa aaaaaa 1455

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<210> 111

<211> 675

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (617)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (647)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (659)

<223> n equals a,t,g, or c

<400> 111

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gtggtttccg cccggcagcc cgcagcccgc tggccgccct tcgtctgggt ctccgcccc 60
aggaccgcg gccgagagct ccggagcgcg gcttccccgg ccggctgcgc gatgggctgc 120
gggaactcca ccgccaccag cgcgggcgcg ggccaaggcc ctgcaggagc agccaaagat 180
gtaacagaag aatccgtaac agaagatgac aagaggagaa actatggagg agtatatgtt 240
ggcctacct ctgaagctgt caatatggtg tccagtcaaa caaagacggt tcggaaaaat 300
tagaagaaaa taacatcatg actcaagaat caagagcttg ctcatcagtt tggaagggaat 360
ttggctccgt gggacgttgt aatgtgcaca gacatttcca aggaaattct aaacagtcac 420
ccttcccttt tgcatccccc caaatcttaa gtgtatacat aaaaccctgg gtacatatattg 480

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ttgtggtaat agaaggggaat tggttaaaaca gtacacttgt ttatgggract ttctgtggcc 540
 acctacgaaa gacaagttac aamctscakg gaggcygttg ttgcccagcc agggggcgcgk 600
 gcattttgac aacattncca ccctggccac tcagcacatt tcatggnggg catgccttnc 660
 actgaacctt ttgat 675

<210> 112

<211> 548

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (521)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (545)

<223> n equals a,t,g, or c

<400> 112

ggcacgagtg aacctccagc tttagcaact catatatcag tctctcacat ggccacaatt 60
 ctagacaaaa accaaagacc cagaggccag agcaaagtag gacctccaca cagcaggtga 120
 tttcccgtgt gacatatattt cttcatagtc cctaataatag tcctcctcta cagagttggc 180
 gtgctgtgtg cactgtggat taggaacaga gtggagctgt aaccagtctc ttctctggcc 240
 ctttgccctt atgtcagctt gcacttttgc ctcacttatt cctagtccag ctcccaactg 300
 cctgacttaa tggaccagaa cggagatttg gatattaaga tgcagarggg gaggggaagg 360
 gatggtagag atagacagct ctcccctact aggttggtgc atttcccta ataactatag 420
 agagactgtg tttcaactct ttttycattg ctgtttccar aagagtggag agtgtggttt 480
 caggcaagggt attaatgata maattccgtg gtattacagc nccctgtgga catttggaag 540
 tttcnttt 548

<210> 113

<211> 476

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (342)

<223> n equals a,t,g, or c

<400> 113

ggcasagagg cgctcggtrct cagcgggtgtt ggaacttcgt tgcttgcttg cctgtgcgcg 60
 cgtgcgcgga catggcctca aacgattata cccaacaagc aacccaaagc tatggggcct 120
 accccaccca gcccgggcag ggctattccc agcagagcag tcagccctac ggacagcaga 180
 gttacagtgg ttatagccag tccacggaca cttcaggcta tggccagagc agctattctt 240
 cttatggcca gagccagaac agtgagtctt tctcagcggg tcacctcttc ctactcttct 300
 tgaatattgc ttttcttttt cttgtttttt ggagacggag tntggctcctg ttgcccaggc 360
 tggagtgcag tgggtgtgtc tcagcttcac tgcaacatca gcctaccggg ttcaaacgaa 420
 tttccctgc ctcagcctcc tgagttagctg ggaattacag gtacctgcta accaag 476

<210> 114
<211> 1016
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (885)
<223> n equals a,t,g, or c

<400> 114
ggagctgcag agaaatttcg tgaacatcgg ccaactaagc tgaagagcct cctgcgcctg 60
gtgaacactg gtaccagcag gcccatcatc ctggatccgg ccgaccccac cctcaacgtg 120
gcagaagggt acagatggga catcgttgct cagagggcct ccagtgccct gaaacaggac 180
tgttgctatg acaacaggga gaaccccatc tccagctgga acgtgaagag ggcacgagac 240
atccacttga cagtggagca gaggggttac ccagatttca acctcatcgt gaacccttat 300
gagcccataa ggaagggttaa agagaaaatc cggagaccag gggctactct ggcctgcagc 360
gtctgtcctt ccaggttcct ggcagtgaga ggcagcttct cagcagcagg tgctccttag 420
ccaaatatgg gatcttctcc cactatcaca tctatctgct ggagaccatc ccctccgaga 480
tccaggtctt cgtgaagaat cctgatggtg ggagctacgc ctatgccatc aacccaaca 540
gcttcacctt ggtctgaag cagcagattg aagaccagca ggggcttcct aaaaagcagc 600
agcagctgga attccaaggc caagtcctgc aggtctggtg ggtctgggga tctatggcat 660
ccaagacagt gacactctca tcctctcgaa gaagaaagga gaggtctctg ttccagccag 720
ttagttttct ctgggagact tctctgtaca tttctgccat gtactcccar aactcatcct 780
gttcaaycac ttgtcccat tgtctactgg gaaggttccc aggtcttcca ccagttttac 840
aatgagttat tcccaggcca gacgtggtag cttcacacct gtaanccag aactttggga 900
ggccgagggtg ggaggagcgc ttgagccgag gagttcaaga ccagcctggg tattataggg 960
agaccccgctc tctacaaaat taaaaaataa tttacaaaaa aaaactgtgc cgaatt 1016

<210> 115
<211> 494
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (366)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (426)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (449)
<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (490)
<223> n equals a,t,g, or c

<400> 115
cggaggctga agaagaagaa aacaaccata aagaaaaaca ctctcaatcc tgtctacaat 60
gaggccatca tctttgacat tccccggaa aacatggatc aagtcagcct gtcctatctca 120
gtcatggact atgatcgagt gggccacaat gagatcatag gagtctgtcg tgtggggatc 180
actgctgaag gcctgggcag ggaccactgg aacgagatgc tggcataccc ccggaagccc 240
atcgcacact ggcactcctt ggtggaggta aagaaatcct tcaaagaggg aaaccctcgg 300
ttgtgatttc attcacgtgg atgctgcaac agaagagact gccacctgga gttaggatgg 360
cagggncgag ctgctagctt cgacagtgag agctcgtgcc catttccgaa accacttcca 420
acaccngaga tgtgcagcca attacacant gggattcagc atgttccttt gcattgttca 480
acgttaaaan gttt 494

<210> 116
<211> 3236
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (8)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (33)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (51)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2923)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3235)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (3236)
<223> n equals a,t,g, or c

<400> 116

ccttttgnaa aaatcgatcc atttggtggt gancctttca aaggttcaga nccatttgca 60
tcagactggt tcttcaggca atctactgat ccttttgcca cttcaagcac tgaccctttc 120
agtgcagcca acaatagcag tattacatcg gtagaaacgt tgaagcacia tgatcctttt 180
gctcctggtg gaacagttgt tgcagcaagc gattcagcca cagacccctt tgcttctgtt 240
tttggggaatg aatcattttg aggtggattt gctgacttca cacattgtca aaggtcaaca 300
atgaagatcc ttttcgttca gccacatcga gctctgtcag caacgtagtg wttacaaaaa 360
atgtatttga ggaaacatcg gtcaaaagtg aagatgaacc ccagcactg ccaccaaaga 420
tcggaactcc aacaagacct tgccctctac caccctggga aagatccatc aacaaattgg 480
attctcctga tcccttttaa ctgaatgatc catttcagcc tttcccaggc aacgatagcc 540
ccaaagaaaa agatcctgaa atattttgtg atccattcac ttctgtact accactacca 600
ataaagaggc tgatccaagc aattttgcca acttcagtgc ttatccctct gaagaagata 660
tgatcgaatg ggccaagagg gaaagtga gaaggaaga gcagaggctt gcccgactaa 720
atcagcagga acaagaagac ttagaactgg ctattgcact cagcaaatct gagatatcag 780
aagcatgaag aattctcttg ttctttggca acaatatagt attcttcttc ctgaatactg 840
aaactattta caatgtgtat caaaactacc tgtgagcatg ggaatacaaa aggtttgaga 900
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aagtgataga tagtggagaa aatttatcac ctaaaatata cccatcagta taaggcaagc 1620
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ccatctttgt ggtttagttt atttactcac ttcatgtttt tcacctataa aattgtcaag 1920
ctagcaaaaa aactcttggt tttttaattg ggagagaaga gacctgccag attatcagac 1980
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ctataaataa attccaaaat atccaattca tttcttcttg aaatgggtgt tggtttgttt 2280
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ctggattaca tagattttta tcttttggtt aaatgtgtat acccctggga ccaacataat 2760
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atgtcttaga gtcgtttgtg gtattttatg ttgttgactc tggctccagg gcctgtgctt 2880
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caaacctcta agttgtagcc tgtaattatg agaacagtaa actttaagta ataataaaga 3060

atcccatcca tatatccaat ttgcaattga gttttgcatg gttctctgat tatgtccatg 3120
 ctgtgtccaa ggaggagtag gtacatacaa tcagcacaga ttaatatatg taaaggggtt 3180
 gggacagcac ctggtataga ataaataata aatgtaaact attaaaaaaaa aaaann 3236

<210> 117

<211> 911

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (25)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (688)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (873)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (910)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (911)

<223> n equals a,t,g, or c

<400> 117

tctctccgga cacaccatga taagnacgct gctgctgtcc actttggtgg ctggagccct 60
 cagttgtggg gaccccaactt acccacctta tgtgactagg gtggttggcg gtgaagaagc 120
 gaggcccaac agctggccct ggcaggtctc cctgcagtac agctccaatg gcaagtggta 180
 ccacacctgc ggagggtccc tgatagccaa cagctgggtc ctgacggctg cccactgcat 240
 cagctcctcc aggacctacc gcgtggggct gggccggcac aacctctacg ttgcgagatc 300
 cggctcgtg gcagtcagtg tctctaagat tgtggtgcac aaggactgga actccaacca 360
 aatctccaaa gggaacgaca ttgccctgct caaactggct aaccccgctt cctcaccga 420
 caagatccag ctggcctgcc tccctcctgc cggcaccatt ctaccaaca actaccctg 480
 ctacgtcacg ggctggggaa rgctgcagac caacggggct gttcctgatg tcctgcagca 540
 gggccggttg ctggttggtg actatgccac ctgctccagc tctgcctggt ggggcagcag 600
 cgtgaaaacc agtatgatct gtgctggggg tgatggcktg atctccagct gcaacggara 660
 ctctggcggg ccaactgaact gtcaggntc tgacggccgg tgkcagggtga cggcatcgct 720
 agcttcgggt ctgcctcgg ctgcaactac taccacaagc cctccgtctt cagcgggtc 780
 tccaattaca tcgactggat caattcgggt attgcaaata actaaccaaa agaagtccct 840
 gggactgttt cagacttgga aaggtcacag aangaaaata atataataaa gtgacaacta 900
 tgcaaatccn n 911

<210> 118
<211> 1977
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (4)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1948)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1958)
<223> n equals a,t,g, or c

<400> 118
cggnacgggtg ggcggccctg agcctgggta ggcggcgcgag ggccgggaga accgttcgcy 60
gaggaaaggc gaactagtgt tgggatggcc accaactggg ggagcctctt gcaggataaa 120
cagcagctag aggagctggc acggcaggcc gtggaccggg ccctggctga gggagtattg 180
ctgaggacct cacaggagcc cacttcctcg gagtggtga gctatgcccc attcacgctc 240
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aacctgctag tggatgctgt cagccagaac gctgccttcc tggagcaaac tctttccagc 360
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gagggcattg ccagactgts wkccctcwgw wtccscwcag actgtgttcc tgggcctgaa 480
tcgctcagac tacatgttcc agcgcaggaa gatggctccc cagccctgaa acagatcgaa 540
atcaaacacca tctctgccag ctttgggggc ctggcctccc ggacccagc tgtgcaccga 600
catgtttctca gtgtcctgag taagaccaa gaagctggca agatcctctc taataatccc 660
agcaagggtg tggccctggg aattgccaaa gcctgggagc tctacggctc acccaatgct 720
ctggtgctac tgattgctca agagaaggaa agaaacatat ttgaccagcg tgccatagag 780
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tacttccggg atggctacat gcctcgtcag tacagtctac agaattggga agcacgtcta 960
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caaaagtttt atggaagggt aaatactggt accttcccc agctttccat ctgaggacca 1680
gaaaagttgt gtctccctta gatgagatct agacgcccc aaatccttga gatgtgggta 1740

```

tagctcaggg taagctgctc tgaggtaaag gtccatgaac cctgccccac tcctgtcagc 1800
ccctcatcag ccttttcagc aggttccagt gcctgacttg ggataggact gagtggtagg 1860
aggaggggga gtggagggca tagcctttcc ctaattctgc cttaaataaa actgcattgc 1920
tgattcaaaa aaaaaaaaaa aaaaaacncg ggggggggnc cggtaccaa ttggcct 1977

```

```

<210> 119
<211> 804
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (99)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (756)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (803)
<223> n equals a,t,g, or c

```

```

<400> 119
ggcacagagg tgatgaaacc acccacagct ttgttggggg tattatattt ctttattttt 60
ttgtttttta gcccatcaca acattgataa ctgatgttna aactgcttga gcatcaggat 120
actcaaagtg gaaaggatca cagatttttg gtatgttctg ggtctacaag gactttccaa 180
atccaggagc aacgccagtg gcaacgtagt ractcaggcg ggcaccaagg caacggcacc 240
attgggtctct gggtagtgtc ttaagaatga acacaatcac gttatagtcc atgggtccatc 300
actattcaag gatgactccc tcccttccctg tctatttttg ttttttactt ttttactctg 360
agtttctatt tagacactac aacatattgg gtgtttgttc ccattggatg catttctatc 420
aaaactctat caaatgtgat ggctagattc taacatattg ccattgtgtg gagtgtgctg 480
aacacacacc agtttacagg gaaagatgca ttttgtgtac agtaaacggg gtatatacct 540
tttgttacca cagagttttt taaacaaatg agtattatag gactttcttc taaatgrgct 600
aaataagtca ccattgactt cttggtgctg ttgaaaataa tccattttca ctaaaagtgt 660
gtgaaaccta cagcatatcc ttcacgsaga gatttycatc tattatactt tatcaaagat 720
tggccatgtt ccactkggaa atggcatgca aaaacnatca tagaaaaaac ctgcgttact 780
ccatctgacc aattccaaag aana 804

```

```

<210> 120
<211> 737
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (707)
<223> n equals a,t,g, or c

```

<220>

<221> misc feature

<222> (713)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (715)

<223> n equals a,t,g, or c

<400> 120

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taactgatca tccaggaaga acaggtagac caacccttcc tggtaaagta actgaggaaa 60
ttgtctcaag tgagcatgat gagggtttat ctttctcagg aaagggtgcag tgctatggta 120
gggagttaaa ccagcctgcc tcagctgcca aatgcacagg tgacttcagt ctttctcctg 180
aaaaactggt aaaatcagga aatccattgc agccagttag tatagagaat agaaatttgg 240
acttaaaaca tcttgtcttg gagtccagtg aacctccatt tggtoctaga aatgttattg 300
aaaataagtc tttgtctgac acattggttt ccacaactgc accaagtggg atagtgaatg 360
tgtcagtaaa acagcagact agccctaaaa gcagtcagaa ccatctcttt cccggtgatt 420
tgaaaacaga tgaaggcatt tatctgcagg tgaagtcctt gacagctgcc tcggttgatg 480
gagcttattc tacacaggga tgcattgtct cagtgggtccc cacgctttgt tcttctcag 540
acaatgctac attaacccat tatgtaagac caataaatgc agagccagcg tttcaagcac 600
agaataccag caggcagaat ggccagtttg cttaagaatg gtgagcctga agctgagtta 660
cataaagaaa ccacaggtcc aggcactgct ggccctcagt ccaacancac atntngtttt 720
aaaaggtgaa cgcaaag                                     737

```

<210> 121

<211> 1252

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (65)

<223> n equals a,t,g, or c

<400> 121

```

agggccctag cagccgggct ggtcctgctg caagccggcg gcccggaagt ggggcgggcg 60
gtgtncctaa ggacagtttt attttaagca attctwagtc tcaagtaaac accatcatta 120
aaagaactga gaactattat caattcttcc tttggagtcc atcttcaatg gaaaggagaa 180
gggaaaacct tttttaaaaa gaagaaagaa aactgaagtt tttgatttga ctagagaaat 240
attcagaaga ctcttatttt tcacctagtc taatcacaaa attgagaaac aaacattatc 300
ccttgaccat gtaaatttta caccacatta tgtcaacagc atgtaccttc cacattgagt 360
attcagaaaag aagtgatctg aactctgacc attctttatg gatacattaa gtcaaatata 420
agagtctgac tacttgacac actggctcgg tgagttctgc ttttctttt taatataaat 480
ttattatgtt ggtaaattta gcttttggtt tttcactttg ctctcatgat ataagaaaat 540
gtaggtttct ctttcagttt gaattttccy attcagtaaa acaacatgct agraacmaa 600
cttttggraa ggcattgtaa ctattttttc aaatagaacc ataataacaa gtcttgctct 660
accctaaagt caaatgctga agattcttta ctgctgtcat cagcatctac aagtagcata 720
ttttggatgg tgtttgtgtg ctacttcaaa gtaactagga aaaaaataat ctcgcaacac 780
aggtaccttg tcatgtcaga attgggggtg ttaggttgcc agttgtatca gtgttgattc 840
atttcattac ttcctacaga gcaaacatga acgttgagat tgcccacagt gaagtgaatc 900

```

```

caaatacccg tgtcatgaac agccggggta tgtggctgac atatgcattg ggagttggct 960
tgcttcatat tgtcttactc agcattccct tcttcagtgt tcctgttgct tggactttaa 1020
caaataattat acataatctg gggatgtacg tatttttgca tgcagtgaag ggaacacctt 1080
tcgaaactcc tgaccagggt aaagcaaggc tcctaactca ttgggaacaa ctggactatg 1140
gagtacagtt tacatcttca cggaagtttt tcacaatttc yccaataatt ctatawtttc 1200
tggcaagttc tatacgaaga tgatccaact cacttcatcc taaacacagg tg 1252

```

<210> 122

<211> 1848

<212> DNA

<213> Homo sapiens

<400> 122

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gcagtaccgt ccgaattccc gggctcgacc acgcgtccgc agctcctgtt ggagttcagt 60
ttctggaatg agcctgtgcc aagatccgga cctaatatat atgaactcag gtcttaccaa 120
ctccgaccag gaaccatgat tgaatggggc aattactggg ctctgtgcaat ccgcttcaga 180
caggatggta acgaagccgt cggaggattc ttctctcaga ttgggcagct gtacatgggtg 240
caccatcttt gggcttacag ggatcttcag accagggaag acatacggaa tgcagcatgg 300
cacaacatg gctgggagga attggtatat tacacagttc cacttattca ggaaatggaa 360
tcagaatca tgatcccact gaagacctcg cccctccagt aaagctgtag agtttctatg 420
tgcctacata catttctgtg acaagtattt gtcgtaaatt aattttaatt gtgtatcaag 480
tgaaaaagaa aacttgaggt ttaagctgc tgtatatagc ttgtgagaaa cctcttttct 540
ttaaaattta cataatcaca agaaaggaaa gaattacagt tggactgatt gtgacagtgc 600
cttgctgctc tctttgaaac acccctgtgt gtccagtata ccttataaca cttagccact 660
tctccccacc ctccagaagg ggtccacgtt gaattctgaa tcctcttgaa aataagattc 720
caaccacaaa aaaaatttag ccatttacka maaawacatt tctgtgacaa gtatttgtcg 780
taaatataatt ttaattgtgt atcaagtga aaagaaacac tgaggtttta agctgctgta 840
tatagcttgt gagaaacctc tttcttttaa aatttacata atcacaagaa aggaaagaat 900
tacagttgga ctgattgtga cagtgccttg tcgtcctctt tgaaacaccc cgtgttgtcc 960
agtatacctt ataacactta gccacttctc cccaccctcc agaaggggtc caggttgaat 1020
tctgaatcat cttgaaaata agattccaac cacaaaaaaa atttagccat ttctttacta 1080
aaaaaaacca aaaaacaaat ctgttttata atcacagatt tttagacaaa tttcttgtat 1140
caggaagaaa tacaattttt gtcatgtttc tcaagcagtt tttctgagta gtttctgagg 1200
aggaacaaat tacaagtgtt cccaataact gaaaatgttt taactcactc tcatttgtaa 1260
cgagtcacac tagtagacaa tgggttttcc aagctgggca aggtacattt aatcagtaaa 1320
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cttggtgtatc atatgtgatt ttgaaatgaa caccttgaat agcactaatt tttatttgtg 1440
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gtgaaagtcc tgttgaaatg aacaattgtc tgccccacaa tcaagaatgt atgtgtaaaag 1740
tgtgaataaa tctcatatca aatgtcaaac ttttcatgtg gaatgatttt ctcaaagaac 1800
atagaaaagt caataaaatc ctcttaattt ccacaaaaaa aaaaaaac 1848

```

<210> 123

<211> 463

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature
 <222> (52)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (59)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (262)
 <223> n equals a,t,g, or c

<400> 123
 ctggtatcat tgagcccaca catggaggaa gcagaactca tcagttcttg gngtttcang 60
 ccatgcctaa cttttccctt gagtgcattg catgttttgt tacaggttgt agagtatttg 120
 cagaaggaaa ccatttctgg ttatttggtt ataaaaagtc agcataaaat atgatccaac 180
 taaaagggat taatttttgg catttttgta tttttatgca ttaggtgatg ggacttttaa 240
 aggtttgaat ttattaggac angaactaaa aataaaagtg cactagggga cagttrattt 300
 maatctaaga aaagttaaca cttgggraat tacaagaagt aaaacaagtg caactaaatc 360
 atttattagt tgttttttga aagcagtttt atgtataaat aacaaatggt tatatttaac 420
 taaatgtaag gtacgaattt tacatattaa acttttcttc ccc 463

<210> 124
 <211> 350
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (321)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (323)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (341)
 <223> n equals a,t,g, or c

<400> 124
 ggcagagtga tagaagaact tgggtgggac gatagaattr aggcatttaca gctgcatgar 60
 aaccgtcaaa ttggccagtc ggcttttraac atcatcgaga agcacttttg tgagaaaacc 120
 tccagaagca acctcctgwa ctcaaagatt aaggaaacag tcaagccaac gaggaaccag 180
 ccgtcggggtc ggggagaaaa aacaacaaaw ttaagcaatg aaaggtttcc aggtcaggaa 240
 cacctggggg ttaggaacag gagcctgcac ccaggttaag cagagagttg atgtcttggg 300
 tttgttttag gagaggggga ntntttggat tagggggggg naatatttac 350

<210> 125
<211> 1584
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (533)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1466)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1494)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1514)
<223> n equals a,t,g, or c

<400> 125
antgaccacc agcatcaacg tccctgccgc ggcctccaag atctccatgc aggagcttga 60
ggaactgagg aagcagcttg gcagcgtggc cacaggetcc acgctgcagc agtctctgga 120
acttaaaaga aagatgcttc gagacaagca gaacaaaaaa aattcaggcc agcacctccc 180
catcttccca gcatgggtgt atgagagacc tgccctgacg ggggatttcc tgattggtgc 240
tggcatcagc acagacaccg ctttgccgat agsacgttgc ccctggcctc gcaggagtcg 300
gccgtggtgg aggacctgct gtacgtgctg gtgggcgtgg acgggaggta cgtcagtgc 360
cagcccctgg ctgggaggca gagccgracc ttctcgtgg accccaacct ggacctgtcc 420
atcagggagc tgggtgcacag gatcctccca gtggccgcca gctactccgc tgtgaccagg 480
ttcattgaag agaagtcttc cttcgagtac gggcaggtga accacgccct ggnggccgcc 540
atgcgcaccc tgggtgaagga gcacctgatt ctggtgtcac agctggagca gctgcacagg 600
cagggcctcc ttctcgtgca gaagctctgg ttctacatcc agccagccat gcgcaccatg 660
gacatcctgg cctccctcgc cacctcgttg gacaaaaggc aatgtcttgg ggggtccacg 720
ctgagcctgc tccacgacag gagcttcagc tacacagggg acagccaggc gcaggagcta 780
tgccctgtacc taaccaaggc ggccagtgtc ccctacttcg aggttctgga gaagtggatc 840
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aaggagagga tccaggagga ttacaacgac aagtactggg accagcggta caccatcgtc 960
cagcagcaga tcccgtcctt cctgcagaaa atggcggaca agatcctcag cacaggaaaa 1020
tatctaaatg tggtcagaga gtgtggccat gacgtcacct gcccgggtggc taaagagatc 1080
atctacacgt taaaagagcg ggcgtatgtg gacgagatcg agaaggcgtt taactacgcc 1140


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agcaagggtgc tgctggactt cctgatggag gagaaggagc tggtggetca cctcagggtcc 1200
atcaagcgct acttcctcat ggaccagggc gacttcttcg tgcacttcat ggacctcgcg 1260
gaggaggagc tccggaagcc ggtggaggac atcacgcccc ctgccttga agcgtcctcg 1320
gagctggcgc tgcgcatgag cacggccaac actgacctct tcaaggacga cctcaagatc 1380
gacctgatgc cccatgacct catcactcag ctcttgcgcg tcctggccat cgagaccaag 1440
caggagaagg cgatggcgca cgcgancccc acggagctgg cgctgagcgg cctnggaggc 1500
yttcttcttt cgantacatc gtcaagtggc ccctttcggg tcattcatcm aamagggtgcg 1560
ggttcggctg cttcggggca actg 1584

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<210> 126

<211> 1304

<212> DNA

<213> Homo sapiens

<400> 126

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cagggcactg agtgattctg gatgggcttc tgacctgggg acaattttaa cagcattaca 60
accgacattt tggttttctt ggggatttta taggccaggt acaaagcaga aagtgcatag 120
aagatgtgat ccactttgcc tgggaagaga agctctttct cctggctgat gaggtgtacc 180
aggacaacgt gtactctcca gattgcagat tccactcctt caagaagggt ctgtacgaga 240
tgggggccga gtactccagc aacgtggagc tcgcctcctt ccactccacc tccaagggtc 300
acatggcgca gtgtggttac agaggaggct acatggagggt gatcaacctg caccctgaga 360
tcaagggccg gctggtgaag ctgctgtcgg tgcgcctgtg cccccagtg tctgggcagg 420
ccgccatgga cattgtcgtg aaccccccg tggcaggaga ggagtccttt gagcaattca 480
gccgagagaa ggagtcggtc ctgggtaatc tggccaaaaa agcaaagctg acggaagacc 540
tgtttaacca agtcccagga attcactgca accccttgca gggggccatg tacgccttcc 600
ctcggatctt cattcctgcc aaagctgtgg aggtgtctca ggcccatcaa atgggtccag 660
acatgttcta ctgcatgaag ctctggagg agactggcat ctgtgtcgtg cccggcagtg 720
gctttgggca gaggaaggc acttaccact tcaggatgac tatcctccct ccagtggaga 780
agctgaaaac ggtgtctgag aaggtgaaag acttccacat caacttcctg gagaagtacg 840
cgtgaggacg cctgagcccc agcggragac ctgtccttgg ctcttcctcc caatgccgt 900
caggctgaac tcgcctcccc cgtgactctg cctcgggcct cgcagaggcc gctggtcact 960
tcgtcatcat tttgcccttg gagacgtctt tctttgtgcc ttgatgttga gagcgctct 1020
cttttgagca aacaagcatt ctatatgcaa ccagagtaga ggggactgct cagcaggtgt 1080
gaccaggggt ctctgaatct gttattgttt ttgcttcttg aaagttcatt tggggtttac 1140
aacaactagg atgtgttggg tgagatgttt cagatcttga gaaatgagca ggtgtcggga 1200
aatgtgtgac ttaaccgtgg tgagggctgg aaatccaaac tcaccaccat gatctgtgaa 1260
ataaagccct tagcggtgaa aaaaaaaaaa aaaaaaaaaa aaaa 1304

```

<210> 127

<211> 901

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (598)

<223> n equals a,t,g, or c

<400> 127

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agcagcgctg ctttttttta cagacactgc ttttcttaca gtcttcgatt ataagcgcca 60
tggctatggc tagtgtaaaa ttgcttgccg gtgttttaag aaagccagat gcctggattg 120

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gactctgggg tgttctccga gggacacctt catcatataca actctgtact tcctggaatc 180
gatacttgta ttttcttagt accaagttac gtgcaccaa ttataaaaca cttttttata 240
atattttctc actgagactc ccagggtctt tactatctcc agaattgtatt tttccttttt 300
ccgtaagact caaaagtaat ataaggctta caaaatctac taaaaagtct ctgcaaaaag 360
tagatgaaga ggactctgat gaagaaagcc atcatgatga gatgagtga caggaagagg 420
agcttgagga tgatcctact gtagtcaaaa actataaaga cctggaaaaa gcagttcagt 480
cttttcggta tgatgttgct ctgaagacgg ggctagatat tgggagaaac aaagtggaag 540
atgctttcta caaagggtga ctcmggctga atgargaaaa attatggaag aaaagcanaa 600
cgggtgaaagt gggagataca ttggatcttc tcattggaga ggataaagaa gcaggaacag 660
agacagttat gcggattctc ttgaaaaaag tgtttgaaga gaagactgaa agtgaaaaat 720
acagagtggg gttacggcgg tggaaaagtt taaagttgcc taagaagaga atgtctaaat 780
aaatggattg ctttttagca atagagctgc tttctagtgg taaaggagg ggtcacctga 840
aaaataggac atttttatta aaataaagtt ctcttagcgt ttgtggaaaa aaaaaaaaaa 900
a 901

<210> 128

<211> 3287

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (46)

<223> n equals a,t,g, or c

<400> 128

cttaaaccgg ggtcgaccgg cccgtccggt gtcctcagg agccangccc cacccttaga 60
aaagatgttt tccatgagga tcgtctgcct ggtcctaagt gtggtgggca cagcatggac 120
tgcagatagt ggtgaagggt actttctagc tgaaggagga ggcgtgcgtg gcccaagggg 180
tgtggaaaaga catcaatctg cctgcaaaaga ttcagactgg cccttctgct ctgatgaaga 240
ctggaactac aaatgccctt ctggctgcag gatgaaaggg ttgattgatg aagtcaatca 300
agattttaca aacagaataa ataagctcaa aaattcacta tttgaatatc agaagaacaa 360
taaggattct cattcgttga ccactaatat aatggaaatt ttgagaggcg atttttcctc 420
agccaataac cgtgataata cctacaaccg agtgtcagag gatctgagaa gcagaattga 480
agtctgaag cgcaaagtca tagaaaaagt acagcatatc cagcttctgc agaaaaatgt 540
tagagctcag ttggttgata tgaacgact ggaggtggac attgatatta agatccgac 600
ttgtcgaggg tcatgcagta gggcttttagc tcgtgaagta gatctgaagg actatgaaga 660
tcagcagaag caactgaac aggtcattgc caaagactta cttccctcta gagataggca 720
acacttacca ctgataaaaa tgaaaccagt tccagacttg gttcccgga attttaagag 780
ccagcttcag aaggtacccc cagagtggaa ggcattaaca gacatgccgc agatgagaat 840
ggagttagag agacctggtg gaaatgagat tactcgagga ggctccacct cttatggaac 900
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<210> 129

<211> 1682

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (24)

<223> n equals a,t,g, or c

<400> 129

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<210> 130

<211> 300

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (300)

<223> n equals a,t,g, or c

<400> 130

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cggccgctct agaggatcca agcttacgta cgcgtgcatg cgacgtcata gctcttctat 240
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<210> 131

<211> 105

<212> DNA

<213> Homo sapiens

<400> 131

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105

<210> 132

<211> 911

<212> DNA

<213> Homo sapiens

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 <222> (63)
 <223> n equals a,t,g, or c

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<220>
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 <222> (861)
 <223> n equals a,t,g, or c

<220>
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 <223> n equals a,t,g, or c

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 <211> 3576
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (2657)
 <223> n equals a,t,g, or c

<400> 133
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<210> 134

<211> 1193

<212> DNA

<213> Homo sapiens

<400> 134

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<210> 135

<211> 1945

<212> DNA

<213> Homo sapiens

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<221> misc feature

<222> (72)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1832)

<223> n equals a,t,g, or c

<220>
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<223> n equals a,t,g, or c

<220>
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<222> (1918)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1924)
<223> n equals a,t,g, or c

<400> 135
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<210> 136

<211> 1146

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (130)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (759)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (790)

<223> n equals a,t,g, or c

<400> 136

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<211> 2345

<212> DNA

<213> Homo sapiens

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<400> 137
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<210> 138

<211> 731

<212> DNA

<213> Homo sapiens

<400> 138

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<210> 139

<211> 757

<212> DNA

<213> Homo sapiens

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<223> n equals a,t,g, or c

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<210> 140
<211> 663
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (558)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (646)
<223> n equals a,t,g, or c

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cgg 663

<210> 141
<211> 3935

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (43)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (68)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1010)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1595)

<223> n equals a,t,g, or c

<400> 141

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<211> 2212

<212> DNA

<213> Homo sapiens

<400> 142

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<210> 143

<211> 743

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (412)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (742)

<223> n equals a,t,g, or c

<400> 143

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<210> 144

<211> 839

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (768)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (812)

<223> n equals a,t,g, or c

<400> 144

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<400> 145

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<211> 1837

<212> DNA

<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>

<221> misc feature

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<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1790)

<223> n equals a,t,g, or c

<400> 146

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<210> 147

<211> 1371

<212> DNA

<213> Homo sapiens

<400> 147

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<211> 1757

<212> DNA

<213> Homo sapiens

<400> 148

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1757

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<211> 3532

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3276)

<223> n equals a,t,g, or c

<400> 149

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111

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<211> 1931

<212> DNA

<213> Homo sapiens

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<220>

<221> misc feature

<222> (314)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1859)

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<222> (1897)

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<220>

<221> misc feature

<222> (1923)

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ttccccccar tcagtattac cctgtgaagc cccttccctc agcagccgcc ttctagttn 1860
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gancgaattt a 1931

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<210> 151

<211> 1631

<212> DNA

<213> Homo sapiens

<400> 151

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ggggatgggg gtatgcagct tggcactggt actgggaggg atgaggggtga agaaggggag 180
aggggtgggt agagatacag tgtgggtggt gggggtggta ggaaatgcag gttgaaggga 240
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tagtaagtgt ttagtggttg ttaagtgtt gcttggagt gagaaagtgc ttagaaactt 360
tccaaagtgc ttagaacttt aagtgcacac agacaaacta acaaacaaaa attgttttgc 420
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cgctcgaaat t

1631

<210> 152

<211> 732

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (729)

<223> n equals a,t,g, or c

<400> 152

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actaagtcca gattccagag cctccagtct ttctgaragt tctcctcca aagcaatgaa 180
gaagtttcag gcacctgcaa gagagacctg cgtggaatgt cagaagacag tctatccaat 240
ggagcgtctc ttggccaacc agcaggtgtt tcacatcagc tgcttccgtt gctcctattg 300
caacaacaaa ctcagtctag gaacatatgc atctttacat ggaagaatct attgtaagcc 360
tcacttcaat caactcttta aatctaaggg caactatgat gaaggctttg ggcacagacc 420
acacaaggat ctatgggcaa gcaaaaatga aaacgaagag attttgagga gaccagccca 480
gcttgcaaat gcaagggaga cccctcacag cccaggggta gaagatgccc ctattgctaa 540
ggtgggtgtc ctkkctgcaa gtatggaagc caaggcctcc tctcagcagg agaaggaaga 600
caagccagct gaaaccaaga agctgaggat cgcctggcca cccccactg aacttggaag 660
ttcaggaagt gccttgagg aagggatcaa aatgtcaaag cccaaatggs ctyctgaaga 720
cgaatcagna ag 732

<210> 153

<211> 494

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (115)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (471)

<223> n equals a,t,g, or c

<400> 153

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atgcagtact ttgtggccaa gaagaaattc cagcaagcgc ggaagcctta cgatgtgagg 180
gacgtcattg agcagtactc gcagggccac ctcaacctca tgggtcgcgt caaggagctg 240
cagaggaggc tggaccagtc cattgggaag ccctcactgt tcacttccgt ctcaaaaaag 300
agcaaggatc gcggcacaac acgatcggcg cccgctggaa ccgagtagga agacaagggtg 360
acgcagtggg accagaggyt ggcactcatc accgacatgy ttcaccagtg gtctccttgc 420
acggtgggca gcacccccgg cagcggcggg cccccccaga gagggcgggg nccacattca 480

acccagcctg gggg

494

<210> 154

<211> 2441

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (12)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2435)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2437)

<223> n equals a,t,g, or c

<400> 154

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gtatgattag gccacaatct tcaatgagta aacatattcc tcaattctgt ggtgttcttg 180
gtcacacatt tatggagttt ctgaagggca gtggagatta ctgccaggca cagcacgacc 240
tctatgcaga caagtgaact gtagaaactg attactgctc caccaagaag ccccataag 300
agtgtttatc ctggacacag aagtgttgaa ttgaaatcca cagagcattt tacaagagtt 360
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tactcaaagc actgagaatt tcaagtggag tatattgaag tagacttcag tttctttgca 540
tcatttctgt attcaatttt ttttaattatt tcataaccct attgagtgtt ttttaactaa 600
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aagtatggag ttaccacaat agtaagagta tgtraagcaa cttatgacac tactcttggtg 780
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tttatcataa aaaaaaaaaa aaaaaaaaaa aaaangncga c 2441

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<210> 155

<211> 2947

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1727)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2109)

<223> n equals a,t,g, or c

<400> 155

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tggatgaggt tcttttttca ggcctacagt caaatctgtg tccagaattt ttgactttt 360
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tctttgcctt ttgatcagaa acttcagcag agcggtaagg attccacatg atttaaaactg 960

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aaatgctttt ctttgttgct gtaagaactt aaaatgtaaa ataccttttt cagtttaagt 1020
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tgactgcccc cttcaaaatc ttcatgtgtg ttacacacca gtgtatttat acaaatcaga 1140
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2947

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<210> 156

<211> 666

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (609)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (614)

<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (638)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (653)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (657)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (664)
<223> n equals a,t,g, or c

<400> 156
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gtggcctatg cagctcctgg cccccggggg atcattatca acctggagaa cggtgagctc 180
tgcataaata gtgccagtg taagagcaat tgctgccagc attcaagtgc gctgggcctg 240
gcccgtgca catccatggc cagcgagAAC agcgagtgt ctgtcaagac gctctatggg 300
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atanct 666

<210> 157
<211> 627
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (144)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (550)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (585)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (624)

<223> n equals a,t,g, or c

<400> 157

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ccttggtacc agctaccccc agggcgaggg ggccccccgc ccggcccagc cccagatgag 480
aagatcaaga gccgtctgga ccctctgcgg gagatgcaga agcatctggg gaagaagaga 540
cagcacggcn gtgatgaagg cagtcgcagc agaaaggaaa agganggggtc tgagaagcag 600
cgaccaagag agcctccatc cctngga                                     627

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<210> 158

<211> 902

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (872)

<223> n equals a,t,g, or c

<400> 158

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<210> 159

<211> 593

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (590)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (592)

<223> n equals a,t,g, or c

<400> 159

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ggcacagagt aagatggcgg cgctgagggc tttgtgcggc ttccggggcg tcgcgggcca 60
ggtgctgcgg cctgggggctg gagtccgatt gccgattcag cccagcagag gtgttcggca 120
gtggcagcca gatgtggaat gggcacagca gtttggggga gctgttatgt acccaagcaa 180
agaaacagcc cactggaagc ctccaccttg gaatgatgtg gaccctccaa aggacacaat 240
tgtgaagaac attaccctga actttgggcc ccaacaccca gcagcgcgatg gtgtcctgcg 300
actagtgatg gaattgagtg gggagatggt gcggaagtgt gatcctcaca tcgggctcct 360
gcaccgaggc actgagaagc tcattgaata caagacctat cttcaggccc ttccatactt 420
tgaccggcta gactatgtgt ccatgatgtg taacgaacag gcctatttct ctagctgtgg 480
agaagttgct aaacatccgg sctcctcctc gggcacatgg atycgagtgt gtttgagaaa 540
atacacgttt gwtgaacaca tcakgctgtg acacacatgc cctggacctn tng 593
```

<210> 160

<211> 1847

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1761)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1765)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1818)

<223> n equals a,t,g, or c

<400> 160

```
gattatcgag gctcccatgg catggcggtc acgttctttg agtaccgagc gtacaggtca 60
attatcaaag actacttcca ccgtggcgcc aagtggacaa cagctcctaa gccacaatg 120
gctgatgagc ttataacca ggattatccc atccactctg tagaagacag acacaaattg 180
gctgctcagg gaaaatttgt gacaactgag tttgagccat gctttgatgc tgctgacttc 240
attcgagctg gaagagatat ttttgacag agaagccagg ttacaaacta cctaggcatt 300
gaatggatgc gtaggcattc tgctccagac tacagagtgc atatcatctc ctttaaagat 360
```

```
cccaatccca tgcataattga tgctaccttc aacatcattg gacctgggtat tgtgctttcc 420
aaccctgacc gaccatgtca ccagattgat cttttcaaga aagcaggatg gactatcatt 480
actcctccaa caccaatcat ccagacgat catccactct ggatgtcatc caaatggcctt 540
tccatgaatg tcttaatgct agatgaaaaa cgtgttatgg tggatgccaa tgaagtcca 600
attcaaaaga tgtttgaaaa gctgggtatc actaccatta aagttaacat tcgtaatgcc 660
aattccctgg gagggaggctt ccattgctgg acctgcgatg tccggcgccg aggcacccta 720
cagtcctact tggactgaac aggcctgatg gagcttgtgg ctggcctcag atacaccta 780
gaagcttagg ggcaaggctt attctcctgc tttaaaaagt gcatgaactg tagtgcttta 840
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ataaagaaaa taacttctgc taggtattac tctctactcc taaagtattt tactatttgg 960
cttcaagtat aaaattttgg tgaatgtgta ccaagaaaaa attagtcacc tgagtaactt 1020
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ttctaaagga gagaaagact tagaacatac acagatccta agtagaacca ggtaattgtc 1260
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ttgtgatata tgctactaaa aaccttttca tatacatctt acctcatttc aagtgaatta 1440
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ctatcagttc ccatccttaa gttttgatat tcaatatctg atagatacac tgcatctttg 1560
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gtatgtgtat ttttattcta ataaactttt gtgttccaga ttgaaaaaaa aaaaaaagg 1740
cgccgctct agaggatccc ncganggggc ccaagcttaa cgccggcatg cgacgtcaaa 1800
gctctctccc caaagtnag tcgtattata agccaggga cgggccg 1847
```

<210> 161

<211> 370

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (363)

<223> n equals a,t,g, or c

<400> 161

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gcccacgcgt ccggtttaga tgtaaacaga caagacagag aggagccttc tgcaaggga 60
gatgaggact ctgactatga ccaacgggtg gcgctctgag ctgctaattg agtcagccgt 120
aaatctgtga aatgacctgt tctttgcaac tgtatttatc aagaaagtca agcgtcctgt 180
aaaatttaga gcatcttgga ggtgggagga agtatccctc ttaccttgac ccctactttt 240
ttttatcttc tttacatttc cagtggaaac cccactttta ttttagaata agaaaattaa 300
gctgagaaca tgagtctgtg ctcttggtat aggggcacct agagtctgtg atccaaagcc 360
ggnattttcc 370
```

<210> 162

<211> 454

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (183)

<223> n equals a,t,g, or c

<400> 162

```
ggcagaggtg ggccactgtt ctgccgctgg ctgggtccct tctataactca gtccccacag 60
gktagtccct ccttcacgct tgggtcctca ctggattcca atgacagtag cttgccctac 120
ggcttactgc tactgttcaa ctctggacat cttgttctcc ttcgctgaat ccctttacaa 180
cgnccacaac tttagtgcc ttcatataaa tgccttcatt tgcactttca gagtagaatc 240
ctgtttcctt ctgaagccct tctaattga tatacttagg gccatcttcc ttaacamccc 300
agacctgctg gtttcggagc catcgaccts ctcatttcca ccgcagargg stggrggaga 360
ttcagaaaat cagggcaggg cccaggagaa agttctttca gagcatggct tcagcctggg 420
tacttctgac accagccagg aagaacagac ttct                                454
```

<210> 163

<211> 1096

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (144)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (182)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1091)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1096)

<223> n equals a,t,g, or c

<400> 163

```
ggagagagag agagagagag agctgggttt ccatccatcc cagtcggcaa gagccccatg 60
gtggagcagg ctgtgcagac tgggtctgct gacaacctga atgctaataa gctgttacct 120
ggcaagggca ccacagggac gcanctcaac ggtcgtcagg cccagccgag cagcaagacg 180
gncagcgatg tagtccagcc ggcagctgtg caagctcaag ggcaggtgaa tgacgagaac 240
agaagacctc agaggaggcg atcaggaaac aggcgaacaa ggaatcgctc cagaggggcaa 300
aaccgttyca ctaacgttaa ggaaaacaca atcaaatttg agggtgactt tgatttcgag 360
agtgc aaatg cccagttcaa ccgagaggag cttgacaaag aatttaagaa gaaactgaat 420
tttaaaagat acaaggctga saagggggaa gagaaggacc tggctgtggt gaccagagat 480
gccgaagcgc ccgctgagga agaccttctg gggcccaact gctactatga caaatccaag 540
tcgttcttcg acaacatctc ttctgaactc aagaccagct ccaggcggac gacgtggggc 600
gaagagagga agctcaacac agagaccttt ggggtgtcag ggaggtttct tcgtggccgc 660
```



```
agttctcggg gcggattccg aggaggcagg ggcaatggga ccacccgtcg caacccact 720
tcccacaggg ccgggactgg caggggtgtga ggggtgcagcc aaaggctcct actgaagtgg 780
cgcataactg acgstgtgtg tktcaggacg cgaggaaaac gctgcactta caggagagg 840
tggtcacttt gtttacggag tttggaagag acccactactg ctacttgtgt tttggactta 900
actgaacttg gacatggctg aagttagaac cacttgtttt ggggaagtat tcatgggtaa 960
cctctttgag gtctctttat ctgtgtttcc tttttagtgt cgcatagcct aattctaagg 1020
ttttgggtatt ttgcaaaaag gtttctatag tgaaagctga atccttactt tgtgactttt 1080
tttttttttt naaggn 1096
```

<210> 164

<211> 2023

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2005)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2016)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2019)

<223> n equals a,t,g, or c

<400> 164

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ggcggggcgc gcgactgctc cgggcggcga tggcggcgga cggggactgg caggatttct 60
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agcctggggc ggaggcgggg gccggggcgg gtgggggcgc cgacggtttc ccggcccygg 180
cctgcagctt ggaggagaag ctgagcctgt gcttccgccc ctcggatccg ggcgccgagc 240
ccccgaggac ggccgtgcgg cccatcacgg agcgcacctc ctgcaggggg acgagatttg 300
gaatgccctg acagataatt atgggaatgt gatgcctgta gactggaagt catcgcatac 360
taggaccttg cacttgctta ctctgaacct ctcaaaaaa ggggtaagtg acagtttgct 420
ctttgataca tcagatgatg aagagctgag agaacagctg gatatgact caatcatcgt 480
ctcctgtggt aatgatgaac ccctcttcac ggcagaccag gttattgaag aaattgaaga 540
aatgatgcag gaatcaccgg acccagaaga tgatgaaacc cctacacagt cagatcggct 600
ttcaatgctt tcccaggaaa ttcaaactct caagaggctc agtaccggca gttatgaaga 660
gagagtgaag aggtctctcag tgtctgagtt aaatgaaatc ctggaagaaa ttgagactgc 720
cattaaggag tactctgagg agctggtgca gcagttggct ttacgagatg aactggagtt 780
tgaaaaggaa gtgaaaaaca gctttatttc tgttcttatt gaagtgcaaa acaaacagaa 840
agagcacaaa gaaacagcaa aaaaagaaaa gaaactaaaa aatggcagct ctcagaatgg 900
gaagaatgag agaagtcata tgcccggcac atatttgact acagtcattc cttatgagaa 960
aaaaaacgga ccacgtctg ttgaagatct tcaaatatta acaaaaattc ttygtgccat 1020
gaaggaggac agtgaaaaag ttccgagctt gttaactgat tatattctga aagttctgtg 1080
tcctacatag agcagcaact ttatctgcgg tgggctccaa gctagatttc cgacagcatt 1140
attctgagag ctggctacca ttacccttct tgctattgga aactcagcac atttgaactt 1200
gggttgatt cagtattaac agatcttgac tacactaatt ctttatatta tagaaccaac 1260
```

ggaaatatgg gcactatddd gaattctaga gatgggtttt gttaaatacta ctaataaaact 1320
gttctcttag tagattaaga gagagtaata ttaattgtgc atgtgcagtt gtatttctca 1380
ttaactgaca gtatgcccat ttgtttttat ggctttctta tctaaactgc actgatgaac 1440
tagattaaag ccttgggaga ttatactat aaattcagtg atggcaagaa ccaacactgt 1500
ttttttgtga gaattgtcag tgtaactatt acctaccagt attgttcaga gagattgaaa 1560
cagaataaac gggctgttct tgaagaagca aaaccagaat atgcattact ttggtttaat 1620
acttagtgct aacattgaaa ctgttggtgg tgatggattt tgtagcttgc tgcttgtttc 1680
accactgggc aaattttaac cattaattg ccattcactt ttagaatctt gtatttaagt 1740
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ctctgaggtg cttgagaaa tgtagactgc agaactgcc attctcatta ctgtgtccta 1860
ttttattcat gcctgtgtgt ttttcttaag tatgaattct agatacagct acttatggat 1920
tcacatcatat catgagcact ttgtgtggt ccagtcaaat caatggcatt taataaattt 1980
ttaagaagt aaaaaaaaaa aaaanggggg gccgcncnng agg 2023

<210> 165

<211> 1320

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1158)

<223> n equals a,t,g, or c

<400> 165

ctctcattgg ctctgctgca scctgacca acgctccaat aggccgggat ccagccatac 60
ttcaatggat cccaggggta tcttgaaggc atttcccaag cggcagaaaa ttcattgctga 120
tgcatcatca aaagtacttg caaagattcc taggagggaa gagggagaag aagcagaagg 180
aggcctgcag tatccctggg attgggaakc ggatggctga saaaatcata gagatcctgg 240
agagcgggca ttgcggaag ctggaccata tcagtgaag cgtgcctgtm ttggagctct 300
tctccaacat ctggggagct gggaccaaga ctgccagat gtggtacca cagggcttcc 360
gaagtctgga agacatccgc agccaggcct ccctgacaac ccagcaggcc atcggctgaa 420
gcattacagt gacttccttg aacgtatgcc cagggaggag gctacagaga ttgagcagac 480
agtccagaaa gcagcccagg cctttaactc cgggctgctg tgtgtggcat gtggttcata 540
ccgacgggga aaggcgacct gtggtgatgt cgacgtgctc atcactcacc cagatggcyg 600
gtcccaccgg gktatcttca gccgcctcct tgacagtctt cggcaggaag ggttcctcac 660
agatgacttg gtgagccaag aggagaatgg tcagcaacag aagtacttgg ggggtgtgcc 720
gctcccaggg ccagggcggc ggcaccggcg cctggacatc atcgtggtgc cctatagcga 780
gtttgcctgt gccctgctct acttcaccgg ctctgcacac ttcaaccgct ccatgagagc 840
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gaacacccat ggctgcaagg tggggcctgg ccgagtgtgc cccactccca ctgagaagga 960
tgtcttcagg ctcttaggcc tcccctaccg agaacctgct gagcgggact ggtgacctat 1020
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ccytccagcc tcagctggct gaacctcgcc gctccaacca ccagcttctt cagcagagcag 1140
ggcccagggc tctgggcntg aaagcaagag ccagcccggc tcccagtgtc tgcccggctc 1200
ccagtgtctg cccagccctc tcccagacag gaacaaggct gscaccctt ctamctyame 1260
actgcccctc cgaaaraatt ttgcaaatk ggccccttgc cccattttta aagcaagggg 1320

<210> 166

<211> 1205

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1027)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1200)

<223> n equals a,t,g, or c

<400> 166

```
gggcactgca ccttacccca cccatccatg ccagcacttc tgcactacgg ccattctcct 60
cttgggcgct cctcagcctc actgtgacct ttctgccaga gctcccagcc aggcctactc 120
tgctgaggtg gcgcttcctg ctaagggcc tctctgccc tttctgccct ccttcccatc 180
ccacatgctg agccgccaca aagaccaaag aagtgatggc tttctctgtg cccctgctgc 240
tctgagggga gaggggtggg tctcctgagc cactcagatg ggaaagtccc ttactcggcc 300
cctccctccc cagcagcccc aagctttaca ctggatgcag cgatcaaccc accactcacc 360
aggcctctcc tccccctgc ccccggtct tagctccagc tgctccaggt agttggttca 420
tccttcccc tctctccctc cctgcttccc cttcagtgt tacttggtc cagccctcca 480
gctgcagccc ctggggaaaa gcagcctccc ttctccttc cctccactcc ctgctccct 540
ccctcagccc ctgtctctgc caggtgcctc ctctcagtca ggcttcagag cagccctgga 600
gacaggaggg ccatgttaaa agctttttca cagttttaag aagacaagtg gagggtgagg 660
atagtgtggt ggggtctggc accatctcat tgctttaatc ccagcaacac aggtggcagc 720
ttctccccct tccttcccac cccagtcctt ctcccaccc ctctcttcta gcttggtaat 780
gaagtatat tatttgtgaa ggaaacagct gctgctgctt ctctgctgc tgggacctgc 840
tccccgtctt cttctccgtg acctttctct agccaggag aaggagagc aggagtattg 900
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gggcaggagc cgagcctttt tgttgycgc tcccaggaga gtgaggggtga cgcaattgat 1140
taaaaccatt ttgttctaaa aaaaaaaaaa aaaaaaaaaa ggggggcgct ctaaaagatn 1200
ctcga 1205
```

<210> 167

<211> 1413

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1376)

<223> n equals a,t,g, or c

<400> 167

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gggatggcgt gtgggtctcc attcgcttgg attctacgct ccgtctctat catgcacaca 60
cttatcaaca tctacaggat gtggacattg agccttatgt aagcaaatg ttaggtactg 120
gaaaactggg cttctctttt gtgagaatta cagctcttat ggtgtcttgt aatcgtttgt 180
gggtggggac aggaaatggt gtcattatct ccatccatt gacagaaacc gtaatcctcc 240
accagggacg tttactgggg ctgagggcaa ataaaacctc aggtgtacca ggaaatcgct 300
```

```

ctggaagtgt aatccgtgta tatggtgatg aaaacagtga taaagtgact ccaggggacat 360
ttataacccta ttgttcaatg gcacatgcac agctttgctt ccatggggcac cgggatgctg 420
tgaaattctt tgtggcagtc ccagggtcaag tcatcagccc acaaagtagc agtagtgga 480
cggatctgac gggtgacaaa gcaggggccat ctgcacagga gcctggtagt cagacgccct 540
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cagaaaggag tcacttgata gtgtggcaag tgatgtatgg caatgagtga gcccatggga 720
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ttcacttcat ttgatggggt cacttgtagt ctgtcactaa taatggaatt aatgggaaac 1080
acttgataaa tgaaactgta ccgttaaata caatagctga gttttcccca gtgtattgta 1140
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atggtatata aaactttgtt ttcacagat ttgggggggt tttatattaa agaaattaa 1320
actacactat ttaaataaac gtttcctgtt tctgacttaa aaaaaaaaaa aaaaanctcc 1380
gggggggggc ccgggaccca ttggggccct tgg

```

1413

<210> 168

<211> 1228

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1178)

<223> n equals a,t,g, or c

<400> 168

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aattcggcac gagctttcca agttgtagt ttgttgttt cagcctgctg ctgctgctgc 60
tgttgcggct aggggaaccg tcgtggggaa ggatggtgtg cgaaaaatgt gaaaagaaac 120
ttggtactgt tatcactcca gatacatgga aagatggtgc taggaatacc acagaaagt 180
gtggaagaaa gctgaatgaa aataaagctt tgacttcaaa aaaagcaaga tttgatccat 240
atggaaagaa taagttctcc acttgtagaa tttgtaaaag ttctgtgcac caaccagggt 300
ctcattactg ccagggtgtg gcctacaaaa aaggcatctg tgcgatgtgt ggaaaaaagg 360
ttttggatac caaaaactac aagcaaacat ctgtctagat gtattgatgg aatttctggc 420
tttctaaatg attttacttt ctgccttgaa ttttcaaggc atagatgtca acttacagaa 480
taacatgttt taagataaatt aagtttaaac cagagaattt gattgttact cattttgctc 540
tcatgttcta aacagcaaca gtgtaactag tcttttgktg taaatggta ttttccttat 600
aagaatttta agaactaagt ggcaaattcc atgaaaatat ttcycrgttc tgkatgcaact 660
tttatttaac attattcata taattctccc cccaccactt tatttataga tactgcaaaa 720
gtgagaagga gataatagat actttgctct gaatttggca tccagagtta acatttctcc 780
cctcactccc ttgctggtgt catagtattt agaatcagca gcctcttaac taattgcggt 840
ttcataggat atataaatgt ttcaagccat tattgtgtaa tggttcttta gttattaacc 900
tagacccaaa tcaaagacca gttggattta tgatattttt ttttgttct tgcagccaaa 960
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aactgaatt ttagaaaaac atattacttt gaattcaaat tgtcatgaaa accagaacag 1080
tgtttgtcca tgttgcattg aatgaaaata aatccctgct ctgagaaaag ctctttgaag 1140
caaaaaccaa actttttttt ttttttttta cctcctgnct tgccccctaa aagaaatmma 1200

```

tagagcaaac atcttgactc tccctttt

1228

<210> 169

<211> 1925

<212> DNA

<213> Homo sapiens

<400> 169

accacgcgt ccgcccacgc tccgatatgt gactgctgat ggtaacattt cttgtatgca 60
gcaggaaaac ctgcaggcta tacgcaaggt atgtgaataa agactgtgga ttgaaggggg 120
aaaagttgat aatacatacc catgataaga attcatattt tctctttctt tgtctcttca 180
tacagaagca agttcgagca gagaaggta gcagttacag cacttaaaag tttaggattg 240
agggtttttg gttgggtttt ttgttttttt gttttttcca tatttcactg ttgctgaaca 300
ttgattttagt ctccaaaat ggacatcact agtaagtga ctgaatactg aaataygctg 360
attggcaagc atatatctgt agctagaatt tttttaaccg taattccaga atttaaaaag 420
gtaagagatc tgctttttga tagaggcctt ttaaaaagac tatataacat ttctatttgg 480
ctgtttatgt gaatgcyag ggaatttgga catgtgtttt atacagaagt ggctttttat 540
atttcttcaa gtgataaatt agcattagga catatcagat agaacaggcc agtttctga 600
tgagattggt agagatgtta cggtaggktc atccttccct tttccatgtt atatgtggag 660
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cgaat 1925

<210> 170

<211> 1558

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1535)

<223> n equals a,t,g, or c

<220>
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<220>
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<222> (1537)
<223> n equals a,t,g, or c

<220>
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<222> (1551)
<223> n equals a,t,g, or c

<400> 170
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<210> 171
<211> 1402
<212> DNA
<213> Homo sapiens

<220>
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<222> (1370)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1400)

<223> n equals a,t,g, or c

<400> 171

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aaagtattta tcatttctac cagaaataaa cgttttaagt ttttacttgn aaaaaaaaaa 1380
aaaaaaaaaa aaaggggggn cg 1402
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<210> 172

<211> 490

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (469)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (489)

<223> n equals a,t,g, or c

<400> 172

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gaattgctcg aactcagggg gtggaggttg cagtgaagtg agattgtgcc attgcactcc 120
agcctgggca acagagcaag actctgtctc aggaaaaaaaa aaaaaaaaaa aagaaaagca 180
acatagtggg gtttctcaat ctgtcctcgg ctgcccttct catttggtga tgggaccttg 240
aaagcaagct tgctaggtgc cctctgtggc tccagccttt accggaagtg tgggtgcatgt 300
ttttaacttc agggaagcgg tatcctgtca ctgggggtatg ggaatgagca tggagaarar 360
agcaccagc cacgaattcc cttccctaag catctcctgt tcctgactgc tccatgaatt 420
gaaaaaaact gacccttggt ttttaaaaaa aaaaaaaaaa aaaaaggng gccccctaaa 480
gaattccanc 490

<210> 173

<211> 1437

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (198)

<223> n equals a,t,g, or c

<400> 173

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cagagtcttg tgctgttccc agaacaggac gacatkaaaa gaacactctt ggaccctaca 180
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<210> 174

<211> 1815

<212> DNA

<213> Homo sapiens

<400> 174


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cagcaagtat tatttgaata aaatgagaaa tgcttaagaa aaattgttgc ccatagtaat 1740
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<210> 175

<211> 971

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (6)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (27)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (961)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (965)

<223> n equals a,t,g, or c

<400> 175

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gttttgaaat catgcatatc attgaaaatt tctcgttttc attttcttag atgacttctt 180
gtctgagaca gaaaaatttc ctactacagc agtgcagtcc agaggttaag atgtattaga 240
attatacaat atcagtttaa aaatctgtat gcataaagaa tgcaccactc aactttttta 300
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gaatataatg gtgcctcca acatttactg ttaaagtgtg ttatctttat atgtcaaaact 900
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nccnnggggg g 971
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<210> 176

<211> 1622

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1394)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1444)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1606)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1613)

<223> n equals a,t,g, or c

<220>

<221> misc feature
 <222> (1618)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (1622)
 <223> n equals a,t,g, or c

<400> 176
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 gcaacaggag tagttcactc cgcgagaggc cgtccacgag acccccgcg gcacatgag 180
 ccccgcccc cgctgttgct tggagagggg cgggacctgg agagaggctg ctccgtgacc 240
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 tn 1622

<210> 177
 <211> 340
 <212> DNA
 <213> Homo sapiens

<400> 177
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 cccgccgag ccgccccttt cctcccctcc ttacgtcccc gagtgcggca gtaccgcctc 180
 cttcccagcc gcgcggcttc ctccagacct ctcggcgcgg gtgggcacca tgtccttgaa 240
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<210> 178
 <211> 616
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (604)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (610)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (613)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (615)
 <223> n equals a,t,g, or c

<400> 178
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 tgggcttgaa ctcacctctg acattagtct gcactcttaa ccacaactta tattgcctgc 180
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 caaaaatggg cttttaatca gagatgtaga aagagtctcw catatttyaa cycttagaga 360
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<210> 179
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 <212> DNA
 <213> Homo sapiens

<400> 179
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 gtgtgcccgt ctgcagaggc acaagatccc ttccaactg tgggacccaa ctcggtcctg 180
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 aggtacgttg gggatcgcaa aaaccagtc tgtcgagaaa tgtccatggc gcttttatcg 360

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<210> 180

<211> 1827

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1524)

<223> n equals a,t,g, or c

<400> 180

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gacatcatca ttcccttacg gactacagag aacaactact gccccacta tgagaagggtg 240
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aacatctact acaagggtctg agtgcccggc acggcctcag gccccgagg gacagtggcg 360
ctggaccgga cctctccttt cgccccaca cccctcccc ttgccagctg tgccaccttt 420
gtatttagtt ttgtagtttc ttggctttta taatccccct ttttccctgc cccctgggct 480
tcggaggggg gtgcttgtgc ccctaaccac catgctcttg tgccctcccc ctctggccag 540
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taaaaaaaaa aaattaacca catggaa 1827

<210> 181

<211> 2026

<212> DNA

<213> Homo sapiens

<400> 181

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taattcatgt atgtattttc acagggtgat agagttgtgt tatttagcca atttaccatg 240
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aatgttgta tacttcacga tattgactgt aatccttata atgacaaaac agcagaagat 480
agatgccata gagtaggcca gactaaagaa gtactagtta taaaactaat aagccaaggg 540
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<210> 182

<211> 456

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (419)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (450)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (453)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (455)

<223> n equals a,t,g, or c

<400> 182

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cccaaattat atatagctct gtttctaagc tctattctgc tctattggac tattgtctgt 120
tcttatgcta atcctacctt attttaagt ctgtgacttt agtcatagga cataccttga 180
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aaattaatag ggagaaagtt gatatcttta tgatatttgt tccatccaag agcatggaat 360
gtctgtatth taaattatca tctatattgg ttattaggtc ttacatatth atgattagnt 420
cctaggthct ttataggatt agggthttgn tgnthg 456

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<210> 183

<211> 481

<212> DNA

<213> Homo sapiens

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<220>
 <221> misc feature
 <222> (4)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (463)
 <223> n equals a,t,g, or c

<400> 183
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 ccaagctcat accttgggtg cagaagatcc tggctgcca ctgagcccgc ggctccctcc 420
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 a 481

<210> 184
 <211> 496
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (60)
 <223> n equals a,t,g, or c

<400> 184
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 gctgcggggc ccccgccatc caccctgtgc tcagcggcct gtccaggatc gtraatgggg 180
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 tcaggacctc cgacgtggtc gtggctgggg agtttracca gggctctgac gaggagaaca 360
 tccaggtcct gaagatcgcc aaggtcttca agaaccctca gttcagcatt ctgaccgtga 420
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 ccgwtgcct gccacg 496

<210> 185
 <211> 1307
 <212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (7)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (383)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1271)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1275)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1279)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1294)

<223> n equals a,t,g, or c

<400> 185

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<210> 186

<211> 449

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (402)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (437)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (440)

<223> n equals a,t,g, or c

<400> 186

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cggtgcgact catgaagggt ttcgtcaccc gcagataccc gccgaggctg tgagggtggag 120
cagtgggact cgatgagcc catccctgcc aaggagctag agcagggtgt ggcgggggcc 180
cacggcctgc tctgcctcct ctccgaccac gtggacaaga ggatcctgga tgcctgcagg 240
gccaatctca aagtcatcag caccatgtct gtgggcatcg accacttggc tttggatgaa 300
atcaagaagc gtgggatccg agttggctac amcccagatg tcctgacaga tamcamcgcc 360
gaactcgcag tctccctgct amttamcamc tgccgccgggt tnccggaggc atccgaggaa 420
gtgaagaatg gtggctngan ctctgggaa 449

<210> 187

<211> 951

<212> DNA

<213> Homo sapiens

<400> 187

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accctgtgt agagggttcc cgctgtgctt ctgagcagtt gctttgttca gaagtgttag 180
gagggtcaga ttgtgccata attgttatta aagagaaaac acgcccacct tcctttctcc 240
cctgctggcc attgttcatt gagtgttact gagggcagcc tttgtggaag tcaggagggt 300

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<210> 188

<211> 381

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (293)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (350)

<223> n equals a,t,g, or c

<400> 188

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agmcertggc agcccttccs gcagctcyga agccactggc aagccccgag gcagggatgg 180
csggcccagg agggaggagg asgacgtcyc tcccgaagar aagaggctgc ggctcttgct 240
ggagrgggga agcgcacagc ccsaggactg cgaggacggg gaggacgcgc cgnggccggg 300
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gggggtccgg ggggtgccggg t 381

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<210> 189

<211> 1309

<212> DNA

<213> Homo sapiens

<400> 189

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tgtagcagct ctttattgct ggagaaggag aaaagtgcc aagatccttt caggatattt 180
ggttttttg ggcgcacaca aatcgagggtg agggaagaga gaggaaaatc ccctgaatcc 240
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aagaaaatga gggaaaacca cagaacatgc caaaggccga ggaagatcgc cctttggagg 360
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cagaaggaaa cccagaggga gggccgaatc agcctggcca gggatttaa gaggacacac 480
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<210> 190

<211> 1899

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (776)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1026)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1887)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1895)

<223> n equals a,t,g, or c

<400> 190

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tcccgtgac cttcagggcc cgggtggcgg gcgcaggccc ctgcggcggc gccgggatgt 180
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tggcgcagaa gctgttagcg ctgaacccag atgcggtgga attgtttaag aaggcgaatg 720
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aggtttcaac ccagagttaa tgtcaagcat gctaatttaa ctagtcactc acagatgact 1800
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aaaaaaaaaa aaaaaaaaaa aaaaaanggg ggggncccc 1899

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<210> 191

<211> 2490

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2484)

<223> n equals a,t,g, or c

<400> 191

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gattgtaggc aaacccacct gtggcatcac tgaaaataaa tttgatcata cctaagaggt 300
taggaaatgg tgccattccc accttagagt gctacatagg tgctttgggc gtatgtaaca 360
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caacacgacc gcgtgtgttg cccctgccct gggctccccg ccatgacatc ttcaccttgc 600
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aaaatctcgg gggggggccc ggtncctatt
2490

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<210> 192

<211> 1808

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1228)

<223> n equals a,t,g, or c

<400> 192

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tattattatt ttttaagaaa gcaagtttca ccgtgcccgg ccaaagtcag ctttcaaaat 180
ccaagccata attggtgagg ggggagtttc agaattacat agaaaaatta atatttgaaa 240
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aagtatagga aaagaactgt ttccttagaa gcggactgtg gaagggtat gtagaatgtc 360
aaagggcaac aagagcctgt gtttttaatg tcatcctgta ctcggcacia atcaaaggcc 420
aatacaagtc tgaaaagcag aaataaatat ttttccaggt ttttgcttg gcacatacta 480
actgcttttg gcattctaatt ctggtctcca aacaccaaag acccatttcg agcctgctat 540
tagcctgctg ctgactctat cacttgagc aataatgtgg ggttatgggt gtggaatctt 600
gtatattttt gtcaaaaata aaaccttgag ttaaggggat agatatagat ggaaaaatac 660
acaaataaat acggtatgaa aacacatgga aatgtgtctt tgtcaaatat gaatcattat 720
taccatcaca aaaattcttc tcttgccaa tatctcattt ccctatatag tatacaagca 780
ccatttcttc tcaattttta agaagagaaa ttagtccatt accacagggg ttcttgtcac 840
tactaattat acaacaatct tttccaaca aaaagatgtc ctccacaacc tttgttttca 900

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aagcagacag catctatgtg gccaaatata ctttgggttg ttcttgagga tactggtttt 960
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ggattgtgct ataatcccta tttagttcaa aattaaccag aattcttcca tgtgaaatgg 1560
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gggaaaagaa tgtctgtagt ggggtgactgt tatcaaatat tttatagaat acaatgaacg 1680
gtgaacagac tggtaacttg tttgagttcc catgacagat ttgagacttg tcaatagcaa 1740
atcatttttg tatttaaaatt tttgtactga tttgaaaaac atcattaaat atctttaaaa 1800
gtagaaca 1808

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<210> 193

<211> 1073

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1028)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1069)

<223> n equals a,t,g, or c

<400> 193

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tttaaaaata tttttctatg tgatgttctg ttcttcaaaa aacaaataca ttaaaaacta 180
ttattgtggg accatattgg cctggaaaaa aaaatctttc ttaattgagc ataaacagga 240
ataaagatta attcaaaata gtttttcctc cttcttttgg aatgtggcat ccccatcaca 300
gttaakgatg taagtttttc aaaactgagt cagggactag tttatcccac aatgcgacaa 360
tgtgggcagg gtaattgtag gttgggctca gttttcttgc cagagttcta atgctgtttg 420
tgtacttacc tctaagtgga ataatttagg tacctataaa gtaagggtc aataacaata 480
accttaatga tggctaatat ttattgaaca tttactgtat gataggaatt tggcaaagtt 540
ttttcatgat cttcacatca actttatgag gtagataata tccacatttt atagctgagg 600
aaactgaaat gtaatgggta aataacttaa ctaggctcac acggacagta aataagctgt 660
atgtccaaga ttacaatcta gacagtttaa ctgtggagcc tgcaccatta attgctatac 720
agtatcataa tcatcaccac caccaccatc cctactgtct ctcagatcga tttttaggat 780
attggttaga tgaacacagag tacatgtgat atatagccaa agctctcttc tctataatat 840
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tactggaaca cagaacagtg ccttgcatatc atacctagga caatatctgg cacaaggtag 960
gcactcaaat attcattgaa ggagtggcaa gatggtaact attcacatca acccccgaca 1020
ggacaccntt ttgcaatggc tataacgcgt cctggcccaa gcctaaaanc cat 1073

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<210> 194
<211> 387
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (67)
<223> n equals a,t,g, or c

<400> 194
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gtccgtnccc ccaggccgct cgcgcaggcg ccgtgcgtaa actggacgca gacgaggacg 120
gcctccccta cctgtgcaact ggctacgacc tgtacgtgac ccgcgagccc tgcgccatgt 180
gcgccatggc cctggtgcac gcacgcatcc tgcgcgtctt ctacggtgcg ccctcgcccc 240
acggcgccct gggcacccgc ttccgcatcc acgcacggsc cgacctcaac caccgcttcc 300
agggtgtccg cggggtgctg gaggagcart gccgctggct ggamcccgc acgtaggcgc 360
cgsccttctg scttcggacc cttcccg 387

<210> 195
<211> 973
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (88)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (89)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (101)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (189)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (895)
<223> n equals a,t,g, or c

<220>

<221> misc feature
 <222> (960)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (969)
 <223> n equals a,t,g, or c

<400> 195
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 agctggctct tttttttaat attttattat ttttgtaac tttattatat gaagggtactg 180
 gaataaaaang aacagacatc cttttctaac tgcactgcct acatgcgtat taagggtccat 240
 tctgcctgtg tgtgctgtgg ctttgaactg taacacctct aatcaattca ggagaaacac 300
 atatcattta aagcaacata ggctaacctg taggtaaacac tgcagtattg atgttttact 360
 gcaaatctta tgggtctaga taatcagtaa aagccatctt ccatagttgg tgtagaaca 420
 ttgccctatt gggttgaca tctgtagaat atatatgaag acaatttctg taatggtttt 480
 aagagattta aaaagaaatt cactggttct ttacaaaata gaatttatca tcaagttatt 540
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 tacgtagtct gtatactcat agggagatgt actgtattat ataacatgta aagttgattt 720
 tcttgtagaca agagaacttc ttttttaac aaggagacat ggcattattt taatttgatt 780
 atggtgagtt gaatttaaga catgaccatg aaggctgctt gtagaattag tgatttttat 840
 taaactatth tttaatgkca acttctctcg ttwatggatt atagagaacc aaaanctatt 900
 actttgggtt tctagaaagg tggtagatat catggcttgg ttaactttat tccttttgan 960
 gaaaatttnc ttg 973

<210> 196
 <211> 643
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (588)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (605)
 <223> n equals a,t,g, or c

<400> 196
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 gcacctgtag tcccagctac tcgggagggt gagagaggag aattgcttga acccagtaag 120
 cagagggtgc agtgagccga gatcatgccca ctgcactgta acctaggtga cagagcgaga 180
 ctccatctca aaagaaaaaa aaaaaatcag aagagttggg ctccagtctc agctgtatca 240
 ttttctaact gattttttaca ataaaaatga gagtaaaaaat cagttactct ttctagacat 300
 taattagcac atttacgtta agactctaag tagtataaaa tgtaaattgc tgctacccta 360
 ctaagttact gtcagtaaat actgtgtgca gtaaatgttg agtatggatt aattgaagga 420

tacctctaca attatttccct ttagtcaagg ttgtagctaa gaattgggct tctgacatac 480
attcttttta atctttttcg tattgggktt tatagcacta aacctaattt ctaacatatt 540
tttacacctg aaatctacat tctaataataa aggttttttt ttataacntt cctaaaattt 600
caggncctca gcaggcagtt tttgtcccag ttttcttcaa cag 643

<210> 197

<211> 452

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (91)

<223> n equals a,t,g, or c

<400> 197

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cctgaccgag gttccctggg aaccagtggg ncgaagggct gagctgtgtg gccagacaag 120
aggtccctgc cctcccccag tgaagccctg ctgttcccgt gggagccatg aagctgaacg 180
agaggagtgt agcccactat gcactcagcg actccccagc ggaccacatg ggcttcctgc 240
gcacctgggg gggcccaggg accccaccga cccccagtgg cactggccga agatgytggg 300
ttgtcctcaa gggcaamctg ctattctyct ttgagagtcg cgagggccgg gcccaytga 360
gcttggtggg gytggaaggc tgcacagtgg aactggccga ggctcccgtg cccgaggagt 420
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<210> 198

<211> 1032

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (41)

<223> n equals a,t,g, or c

<400> 198

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gcagcacccc cgggggaaag acattttctg ctcccaccga gttggcaggg cctgcttcct 120
gaatctcctg ggtgtgtctt aactgccagt cccagcacct cctgaaagcc ccactctcct 180
ccagtgggtca cagtggaagg atcatgggag aaacagaagg gaagaaagat gaggctgayt 240
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tactgccggg aagtgtcggc cgtccttgtc attagtggc atatgaaaat ggccccaaga 960
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ttcaccacga gg 1032

<210> 199
<211> 2732
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (2190)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2680)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2694)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2701)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (2726)
<223> n equals a,t,g, or c

<400> 199
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accaggggc cagggtggct cttctctccc caccctcct tggtctcca gcacttcctg 180
ggcagccacg gccccctccc cccacattgc cacatacctg gaggtgacg ttgccaaacc 240
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tgatcttcca ggggtgggag gagaaaatcc cacctcccct gacctccacc acctccacca 420
ccaccaccac caccaccacc accactacca ccaccacca actggggcta gagtggggaa 480
gatttcccct ttagatcaaa ctgcccctc catggaaaag ctggaaaaaa actctggaac 540
ccatatccag gcttggtgag gttgctgcca acagtcttg cctcccccat ccctaggcta 600
aagagccatg agtcctggag gaggagagga cccctcccaa aggactggag acaaaaccct 660
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<210> 200

<211> 2315

<212> DNA

<213> Homo sapiens

<400> 200

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2315

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<210> 201

<211> 890

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (659)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (828)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (887)

<223> n equals a,t,g, or c

<400> 201

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tcaggccccc gccatggctc cagttggccg actgagactt gcctgggtag ccataaagac 240

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tctgacttcc tcagccacct caccatttc ccacctccca ggttccttga tggagccggt 300
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<210> 202

<211> 1533

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (863)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (872)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (911)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1522)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1524)

<223> n equals a,t,g, or c

<400> 202

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aatgaagaa attggtaaat tgtagccaa ggtggaacaa ctaggagctg aaggggaatgt 420
ggaggaatcc cagaaagtaa tggatgaagt agagaaagca cgggcaaaga aaagagaagc 480

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<210> 203

<211> 2826

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (285)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2755)

<223> n equals a,t,g, or c

<400> 203

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tagaaccgcc agcccgcgtc cgaaggcgga ggcgagggga actggccgcg tgaggggcct 180
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gtatta 2826

<210> 204

<211> 1538

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (3)

<223> n equals a,t,g, or c

<400> 204

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tgccaacatg tcacctgtgt ttatgtaaaa ttgtttagg ttaataaata tattctttgt 300
cagggattta acccttttat tttgaatccc ttctatttta cttgtacatg tgctgatgta 360
actaaaacta attttgtaaa tctgttggct cttttwattg taaagaaaag cattttaaaa 420


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<210> 205

<211> 2342

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2338)

<223> n equals a,t,g, or c

<400> 205

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2342

<210> 206

<211> 827

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (282)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (442)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (802)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (807)

<223> n equals a,t,g, or c

<400> 206

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<210> 207

<211> 2326

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (404)

<223> n equals a,t,g, or c

<400> 207

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<210> 208

<211> 1462

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1445)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1453)

<223> n equals a,t,g, or c

<400> 208

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1462

<210> 209

<211> 2581

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2090)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2566)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2572)

<223> n equals a,t,g, or c

<400> 209

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<210> 210

<211> 1994

<212> DNA

<213> Homo sapiens

<400> 210

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aaaaaaaaa aaaa 1994
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<210> 211

<211> 1514

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (691)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (866)

<223> n equals a,t,g, or c

<400> 211

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<210> 212

<211> 483
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (444)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (469)
<223> n equals a,t,g, or c

<400> 212
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tcg 483

<210> 213
<211> 883
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (869)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (870)
<223> n equals a,t,g, or c

<400> 213
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accctccac ctaatgatcc ccatggatc cagagagaag acctcatcct gagtcttcgc 660
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<210> 214

<211> 4799

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1164)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2403)

<223> n equals a,t,g, or c

<400> 214

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<213> Homo sapiens

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<222> (965)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (987)
<223> n equals a,t,g, or c

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<211> 1164
<212> DNA
<213> Homo sapiens

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<210> 217

<211> 1594

<212> DNA

<213> Homo sapiens

<400> 217

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1594

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<210> 218
 <211> 1545
 <212> DNA
 <213> Homo sapiens

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 <221> misc feature
 <222> (1512)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (1525)
 <223> n equals a,t,g, or c

<220>
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 <222> (1544)
 <223> n equals a,t,g, or c

<400> 218
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<210> 219
 <211> 462
 <212> DNA

<213> Homo sapiens

<400> 219

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<210> 220

<211> 3094

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<400> 220

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atgttttaag gcaaaacaac caactttgtc tgtagtcttc attttctgtg tgggggggga 3000
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<210> 221

<211> 1756

<212> DNA

<213> Homo sapiens

<400> 221

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atccaaatct cctcccaaag tgcccattgt gattcaggac gatagccttc ccgcggggcc 180
ccctccacag atccgcatcc tcaagaggcc caccagcaac ggtgtggtca gcagcccaa 240
ctccaccagc aggccacccc ttccagtcaa gtccctagca cagcgagagg ccgagtacgc 300
cgaggcccgg aagcggatcc tgggcagcgc cagccccgag gaggagcagg agaaacccat 360
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cagacagcct ttgggtcctg atgggtctca aggcttcaa cagcgcagat aaatgcaggc 480
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tcccccttgc tccgcccact gtgacctga accccatgca ctgtgacctc cccccttctc 660
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cacttaaaaa gtaagttcca ttgaaaaata tcctttcttt tttttttctt cctatttttg 960
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aaaaaaaaaa actcga 1756

<210> 222

<211> 571

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (478)

<223> n equals a,t,g, or c

<400> 222

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tgagctctgc cgggacatgt tctccaaaat ggccacttac ctgactgggg aactgacggc 180
caccagtga gactataagc tcctggaaaa tatgaataaa ctaccagct tgaagtatct 240
tgaaatgaaa gatattgcta taaacattag taggaactta aaggacttaa accagaaata 300
tgctggactg cagccttattc tggatcagat caatgtcatt gaagagcagg tagcagctct 360
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gctggagaag cgatgagaaa cttatttcta tgggacagaa gtcttttttt tttaatgnng 480
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attatgtggc atcacaggac attttaacgg t 571

<210> 223

<211> 1697

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (221)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1084)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1320)

<223> n equals a,t,g, or c

<400> 223

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tgatgatgat gatgaagagc atggagcccc tctggaaggg cctatgacct tgcagactat 600
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aatttctgag atccccatgga ggtagattg ggaggaaagc ttaaaagatg tcctttttgt 1620
gagagggatg gaattgtttt ctttcattcg taaagttagt gagtaaagat tttataaatc 1680
aaatgctcta aaaaaaa 1697
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<210> 224

<211> 2156

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2155)

<223> n equals a,t,g, or c

<400> 224

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agagtaacta gcaattttat cttttattca ataaggaagc actaagtaat atggatgatt 180
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gggggtgtgc aattccttgc cagggtgtcc tgggtgacaga cggctgtcctt ggcatttgta 300
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cactaccttt tcctttccca tctaagttat atatcatgtg catggcgaat ttggaggagc 420
tccagagcac cgattccttg gaatgccttg aacgtctcat agatttaaac aatgggtgaag 480
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<210> 225

<211> 1791

<212> DNA

<213> Homo sapiens

<400> 225

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accacggcag atgaacgtgt atcacttcaa gaaaggcaca gagatctgta attacagcta 240
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tgcaaaccca acaggtctat gtgctctctc tatcaacat tccaattctt acctggccta 420
tcctggaagc ctgacttcag gggagattgt gctttatgat ggaaactccc tgaaaacagt 480
ctgcactatt gctgcccatt agggaacact agctgccatc accttcaatg cctcaggctc 540
caaactagca agtgcgtctg aaaaaggcac agtcatccgg gtgttctctg tccctgatgg 600

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<210> 226

<211> 1525

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (44)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (591)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (601)

<223> n equals a,t,g, or c

<400> 226

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cacgcccatc atggtgacta aggtggccga gcggggcaaa gcaaggacgc tgacctccgg 180
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aaaaaaaaa aaaaaaaaaa aaaaa 1525

<210> 227

<211> 1611

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (840)

<223> n equals a,t,g, or c

<400> 227

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atagcaagat aacaattttg agatgagaat gaatagtga cttgctgatt ctgtagcaaa 180
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<210> 228

<211> 1639

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1267)

<223> n equals a,t,g, or c

<400> 228

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tcgctgtttc ggttttcctg gtcctcgggc ccttttctcc cctgttgacg ctgggagcgg 120
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cagaccaa atacaattt atatcaacaa tatgaatgac aaaattaaaa aggaagaatt 240
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aatgccttg agacagctac aaggatttcc attttatggt aaaccaatgc gaatacagta 420
tgcaaaaaca gattcggata taatatcaaa aatgcgtgga acttttgctg acaaagaaaa 480
gaaaaaagaa aagaaaaaag ccaaaactgt ggaacagact gcaacaacca caaaacaaaa 540
gcctggccag ggaactccaa attcagctaa taccacagga aattcaacac caaatcctca 600
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caggactgtt ctaaggttaa tatgcaatct ctttattgaa agacctccag ggtaaaatt 1560
tttgatcta tagtctctt tccccctaa gacaaataga ctgattaata aagagttgcc 1620
agtgtctaaa aaaaaaaaaa 1639

<210> 229

<211> 1083

<212> DNA

<213> Homo sapiens

<400> 229

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cagtgcgcgg agtctgaggt cgctgtggac tgccactgg tttgagacgg taacatctgt 60
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ccagaagatg tttagctaag gccttgcccg agatggacag ccggattcct tatgatgact 180
accgggtggg tttcttgccct gcctatgaga atcctccagc atggattcct cctcatgaga 240
gggtacacca ccggactac aacaatgagt tgacccagtt tctgccccga accatcacac 300
tgaagaagcc tcctggagct cagttgggat ttaacatccg aggaggaaaag gcctcccagc 360
taggcatctt catctccaag gtgattcctg actctgatgc acatagagca ggactgcagg 420
aaggggacca agttctagct gtgaatgatg tggatttcca agatattgag cacagcaagg 480
ctggtgagat cctgaagaca gctcgtgaaa tcagcatgcg tgtgcgcttc tttccctaca 540
attatcatcg ccaaaaagag aggactgtgc actagaaagt tgcagccac agcccttcat 600
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tccctggaat agtgagttgg gaggatgggg agacagctaa ccaactgcat taccctaaacc 720
atattgcact tttagtcccc tagttttcta ggtgagcttc attccctgaa aggaggatga 780
tgatatctag gcataaccta gcctgtgagg aacctagtta ggaaagacaa ctgacattta 840
ttgaatatca tgcactagtc cttacatat gtcatatttt aattatagaa atcagtagca 900
aaaagaatct tggggatttt ccatctgact tccctggcca tcttatccca tccttgact 960
accagaagat tcatacactt ttgagactcc agtgagacgc tgttttcacc ccttcctcct 1020
cctagcctct ctcccaaaaa gtaaacaca atgctgaaga aaaaaaaaaa aaaaaaaaaa 1080
aaa
```

1083

<210> 230

<211> 359

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (246)

<223> n equals a,t,g, or c

<400> 230

```
gtgacggagc gcggtgcgcg cggcagggcc cggagtatcc cgctttcttt ggaggaaacc 60
accgcatcag atctgcgctg cggcagaggc aggcaagtcc ctagecgtgga ggggcagcat 120
gctggcagca cttggggagg cgggtgcgcta agggattcac gctgtaactg ggaccgcagc 180
agggaaactac aatttccata gtgctccgcg ccctcccagc tggtcttact gccggcgacg 240
cgttgngtac acytggggat ttgttagtct tacatggstt tgcgcctcct acctggaagc 300
gggccagcga ttggtaccag ttcagacatg ggtacacggt tgaacagggc cgccgcctt 359
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<210> 231

<211> 355

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (333)

<223> n equals a,t,g, or c

<400> 231

```
ggcagagggt ttctttctca taagaatgaa atcttggaaa ttgctctgga tcaaaaagga 60
```

```

cttaccaatg atagaaaaat tgctttcatt gataaaaaata gagatctctg tatcacttct 120
gtgaaaggat ttgggaagga agaacaaatt atcaagcttg ggaacaatgg tgcatacttt 180
ggcatggaac gatacatgca atatcctttg tggacttcaa gatactcgat ttatagtgtg 240
gtattacccc aatacagttt atgtggacag agacattttg cctaaaacat tatatgaaag 300
ggctgcaagt ggaatttagt gaaaaatgcc ccntattgtg gagttttgtt gggaa      355

```

<210> 232

<211> 374

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (287)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (323)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (332)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (334)

<223> n equals a,t,g, or c

<400> 232

```

ggcagaggga ggcctgggcc tctctgcctg ctgtagccgt ctgccgcgcc cttgttcctg 60
cagctgtcca gttatctttt gactgccaca tatggacccc aaaagatctc aaaaggaaac 120
tgtcctcatt acaggaggaa gtggctatth ttgttttcgc ctgggctgtg cctgaaacca 180
aaatggagtc catgtgattc tgtttgacat cagcagccct gctcaaacca ttccagaagg 240
aatcaagttt atacaaggag acatccgccca cctgtctgac gtrgagnaaa gccttccagg 300
atgcagacgt camttgtgtg ttncawatt gncncttatg gtaatgttca gggcgggagc 360
aaactcaatc gaaa                                     374

```

<210> 233

<211> 432

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (288)

<223> n equals a,t,g, or c

<400> 233

```
aaaaaccaa aaaaaaatt tttgaaccaa acaaggggaa aaaaaggagt tggggcaaaa 60
caggaggcgt ttccctaccc gcatacatcc ccgtccccga gacacccaat cccccaccc 120
ccagcctgcc cgcgcctccc gccccagct cctcgccctg gggacagctg gcagccccgc 180
gcggaccaga cacaaagccg atcaatcccc gaggcgtggg ggcggaggga cgaccgccc 240
gggctttccc gggcgtgct ctctcctgc tgccccctcg ctaggacncg gcggacgcct 300
cgtctggttt tcacgcctc tagccctac cccacaccc ccaaacaga acagaccccc 360
atccctgggc tggaggaccc gcctcttggc agccagctga gaaggcgccc cggggagggg 420
gaaacctctg cc 432
```

<210> 234

<211> 366

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (192)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (251)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (320)

<223> n equals a,t,g, or c

<400> 234

```
gggcagtagg agtatgcagc cctccccaga cacctgamcc tgctggtgcc ttgatcttgg 60
acttcccagc ctctgaagc atgaggacag aaatttccgt gctgtataga ttaccacgcc 120
tatgctgttc tgttattctt camaagcaga tggagacgga cggatcagca mctccacam 180
ggggaactga angacggggc gaggtcagcc cggcaatagc aaaccaggcc aggggcgggg 240
gtggctgaca ncaggcaggg gggttactag gaacaggtca tgaaaggccc tcttacagag 300
gtgggcctgc agcaggcatn agcttaaagg atgggtttgg agcttcagtg tgggttgag 360
ccagag 366
```

<210> 235

<211> 428

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (370)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (383)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (405)

<223> n equals a,t,g, or c

<400> 235

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gtcacgagct cgtgcactct acgggaggggt agctccagct gcagccagag tgtggccctg 60
aagacatcag agagcagggc actcccacct gagagggagg gggaacaaaa ggagaagcct 120
agagcaggca gggcttgctt tgtttggttg tttggttttt ttagttttat tttctttttc 180
agagaagaca gtttcaagct ctctctaag taaggtggga gccactggag ggcataaact 240
gaggcgtgag atgttatgat ttactaatga acaagatcac tctggccact gagataggag 300
tgggaccaca agaaggaagg gttagaaggy tgttgattc accaagccaa grgttgwtgg 360
cgtttgaacn ggggctttac agnaaaaagg gttccaaaaa gtttnatttc tggatatattt 420
gaagttgg 428
```

<210> 236

<211> 966

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (896)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (956)

<223> n equals a,t,g, or c

<400> 236

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cggacgcgtg gggatgctcc ggctgctcag ttccctctc cttgtggccg ttgcctcagg 60
ctatggccca cttcctctc rcycttcag ccgcgttgtc matggtgagg atgcgggtccc 120
ctacagctgg ccctggcagg tttccctgca gtatgagaaa agtggaagct tctaccacac 180
gtgtggcggg agcctcatcg ccccgaytg ggttggtgact gccggccact gcatctcgag 240
ggatctgacc taccaggtgg tgttggtgta gtacaacctt gctgtgaagg agggccccga 300
gcaggtgatc cccatcaact ctgaggagct gtttggtgat ccactctgga accgctcgtg 360
tgtggcctgt ggcaatgaca tcgccctcat caagctctca cgcagcgccc agctgggaga 420
tgccgtccag ctgcctcac tccctcccg cgggtgacatc cttcccaaca agacaccctg 480
ctacatcacc ggctggggcc gtctctatac caatgggcca ctcccagaca agctgcagca 540
ggcccggtg cccgtggtgg actataagca ctgctccagg tggaactggt ggggttccac 600
cgtgaagaaa accatggtgt gtgctggagg gtacatccgc tccggctgca acggtgactc 660
tgaggagacc ctcaactgcc ccacagagga tgggtggtgg cagggtccacg gtgtgaccag 720
ctttgtttct ggctttggct gcaacttcat ctggaagccy acrgtggtca ctcgagtctc 780
cgccttcac gactggattg aggagaccat agcaagccac tagaaccaag gccagctgg 840
cagtgtgat cgatcccaca tcctgaataa agaataaaga tctctcagaa aattcnaaaa 900
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaangggg 960
ggggggg 966
```

<210> 237
 <211> 697
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (473)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (693)
 <223> n equals a,t,g, or c

<400> 237
 ctatctgtgg agctgcccc acaatggctg gctctccac aactgtggcc atcatgaaga 60
 cgctggtgtc atctgctcag cttcccagtc ccagccgaca cccagcccag acacttggcc 120
 aacctcwrt gcatcaacag caggatctga atccacttg gccctgagac tggatgaatgg 180
 aggtgacagg tgcgaggcc gagtggaggt cctataccaa ggctcctggg gcaccgtgtg 240
 tgatgactac tgggacacca atgatgccaa cgtggtctgc aggcagctgg gctgtggctg 300
 ggccatgtca gcccaggaa atgccagtt tggccagggc tcaggacca ttgtcctgga 360
 tgatgtgcgc tgctcaggac acgagtctta cctgtggagc tgccccaca atggctggct 420
 ctcccacaac tgtggccatc atgaagaygc tgggtgtcatc tgctcagctk cyncagtccc 480
 agtcracrc caggccagat acttggctga ccaccaactt accggcattg acagtaggat 540
 ctgaatccag ttgtggtctg argctggtga atggaagtga cagtgtcgar gccgagtgga 600
 ggtcctgtat cgaggctcct ggggaaccgt gtgtgatgac agctgggaca ccaatgatgc 660
 caatgtggtc tgcaagcagc tkgggtgtgg ctnggcc 697

<210> 238
 <211> 2267
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (250)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (824)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (2267)
 <223> n equals a,t,g, or c

<400> 238
 ccgtgccctg cccgcccggc cacttcccgc ccatgagccc cgacttcacc gtcttcatga 60

tcaagtacct gatgaccatg atcgtcggca tcaccactgg cttctggatc tggtcgggca 120
agaccctgca gtygtggcgc cgcttctacc acagacttag ccacagcagc wagggggaga 180
ctgcggtatg agccccggcc cctccccacc tttcccaccc cagccctctt gcaagaggag 240
aggcacggtn agggcaaaaag aactgctggg tgggggacctg tttctgtaac tttctcccc 300
tctactgaga agtgacctgg aagtgaagaa gttytttgca gatttggggc gaggggtgat 360
ttgaaaaaga agacctgkgt ggaaagcggg ttgggatgaa aagatttcag gcaaagactt 420
kcaggaagat gatgataacg gcgatgtgaa tcgtcaaaag tacgggccag cttgtgccta 480
atagaagggt gagaccagca gagactgctg tgaagtttct cccggctccg aggtgaacg 540
gggactgtga gcgatcccc tctgctcagg cgagtggcct gtccagaccc ctgtgaggcc 600
ccgggaaagg tacagccctg tctgcggtgg ctgctttgtt ggaaagaggg agggcctcct 660
gcggtgtgct tgtcaagcag tgggtcaaacc ataactctct ttcactgggg ccaaactgga 720
gccagatgg gttaatttcc agggctcagac attacggctc ctccctccct gccccctccc 780
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aaagcagcgc aaatctgagg tttcccggtg gttgttaatt tgggtgagat aaacattcct 1200
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<210> 239

<211> 767

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (748)

<223> n equals a,t,g, or c

<400> 239

gtgcaaaatc agagaggggt gcaagatcct gatttttcag gagttcaagc gacaatggca 60
gcccaatacgc gcagtatgag cttcaacccc agcacaccag gggccagtta tgggcctgga 120

```

agcaagagcc cagaaattcc caattgagaa ttgtgttagt gggtaaaacc ggagcaggaa 180
aaagtgcac aggaaacagc atccttgcc ggaaagtgtt tcattctggc actgcagcaa 240
aatccattac caagaagtgt gagaaacgca gcagctcatg gaaggaaaca gaacttgtcg 300
tagttgacac accaggcatt ttcgacacag aggtgcccaa tgctgaaacg tccaaggaga 360
ttattcgctg cattcttctg acytccccag ggcytcatgc tctgtcttct ggtggttcca 420
ctgggccggtt aactgagga agagcacaaa gccacagaga akatcctgaa aatgtttgga 480
gagagggcta gaagtttcat gattctcata ttcacccgga aagatgactt aggtgacacc 540
aatttgcatg actacttaag ggaagctcca gaagacattc aagacttgat ggacattttc 600
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gcaccagttg ctgggcctga tccagcgctg ggtgaggag aacaagggaag gttgttacat 720
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```

<210> 240

<211> 1718

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (71)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1505)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1632)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1656)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1715)

<223> n equals a,t,g, or c

<400> 240

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taaaagatgt ntgatcagac ctttctcggt aatgtatttg gctcatgtga caaatgtttc 120
aaacaacgag ctctgagacc agttttcaag aagtctcaac aactcagcta ctgttcaaca 180
tgtgcagaaa ttatggcaac cgaggggctg caccgagaac agacgctggs tctgtgaaga 240
gcgaggccga gagcctcaag ggcaagctgg aggaggagcg agccaagctg caccgatgtgg 300
agctgcacca ggtggcggac ggtgaggagc cctggggcag tttgtcatga agaccagaag 360
gaccctcaaa ggccacggga acaaagtcct gtgcatggac tgggtgcaaag ataagaggag 420
gatcgtgagc tcttcacagg atgggaaggt gatcgtgtgg gattccttca ccacaaacaa 480

```

```

ggagcacgcg gtcaccatgc cctgcacgtg ggtgatggca tgtgcttatg ccccatcggg 540
atgtgccatt gcttgtgggtg gtttggataa taagtgttct gtgtaccctc tgacgtttga 600
caaaaatgaa aacatggctg ccaaaaagaa gtctgttgct atgcacacca actacctgtc 660
ggcctgcagc ttcaccaact ctgacatgca gatcctgaca gcgagcggcg atggcacatg 720
tgccctgtgg gacgtggaga gcgggcagct gctgcagagc ttccacggac atggggctga 780
cgtcctctgc ttggacctgg cccctcaga aactggaaac accttcgtgt ctgggggatg 840
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gtagaattca gcaagttaat atattccata ttatttcttt gaatcaattc attttcagaa 1620
gcactttaaa gncatgatatt tctcgatgtg cactgngatg cctggaacct ttctttggga 1680
aggctgattt atggactgag gatggtgatg gctngat 1718

```

<210> 241

<211> 3599

<212> DNA

<213> Homo sapiens

<400> 241

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gtccacgccc ccgttacctt cgccaggagc ttcaggtcct ctctctccc cgccagtg 180
gagaccccca cctccagtga gggaccgccc aggcgatca gggccctcc caccacctc 240
tccagtaagc agaaacggca gcacatctcg ggccctgcct gctacccctc agttgccatc 300
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cagtgtctgg gacactcccc cacctccacc atcaacatct attagaaatg gcttccaaga 420
ctctccatgt gaagatgagt gggaaagcag attctacttc catccgattt ccgatttgcc 480
acctccagag ccatatgtac aaacgaccaa aagttatccc agcaaactgg caagaaacga 540
aagccggagt ggatccaacc gaagagaaag ggggtgctcca ccaactccct ccatcccgag 600
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ccaaccaa at tcaaacattc actgcttatt tgttacagac tgtaattatt aaagtcctg 960
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tccaatcttt ggcagtcgga gcttggctct aggacagagc tgtccaatag aaatataatg 1140
tgagcccat atacaatttt tacatttcta atatatatta aacaagtga gttaatatgc 1200
atccaaaata tttcaacctg taatcaacat aaaattttta tgagatattt tatattattt 1260
tttggtagct aatcttcaaa atccagagtg tattttacac ttaccgcaca tctccattca 1320
gactagtcac atttttaagt gctcagtagc cacatgtggc tgggtggctac tggattagac 1380

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<210> 242

<211> 2887

<212> DNA

<213> Homo sapiens

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<221> misc feature

<222> (2819)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2850)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2883)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2885)

<223> n equals a,t,g, or c

<400> 242

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<210> 243

<211> 1253

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (109)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (415)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1059)

<223> n equals a,t,g, or c

<400> 243

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<210> 244

<211> 1602

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (7)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1579)

<223> n equals a,t,g, or c

<400> 244

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<210> 245

<211> 1284

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (21)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (63)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (73)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (170)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1229)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1272)

<223> n equals a,t,g, or c

<400> 245

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<210> 246

<211> 2094

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2086)

<223> n equals a,t,g, or c

<400> 246

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<210> 247
<211> 1019
<212> DNA
<213> Homo sapiens

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<221> misc feature
<222> (6)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (111)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (879)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1010)
<223> n equals a,t,g, or c

<400> 247
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<210> 248
<211> 1500
<212> DNA
<213> Homo sapiens

<220>

<221> misc feature
<222> (999)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1065)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1280)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1343)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1400)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1463)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1496)
<223> n equals a,t,g, or c

<400> 248
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ccgcgccacg gctctcccc acaccgctt attcgggtcg agacccggg gccccggcg 180
ccgcctgctg atgagcggat ctccggaccc ccgcccagca gcgataggct agctatccta 240
gaagactatg cggaccggtt tgatgttcag gagactggcg aaggctcagc aggagcttca 300
ggagccccag agaaggtccc tgaaaatgat ggctacatgg agccctatga ggctcaaaaag 360
atgatggccg agatccgggg ctccaaggag acagcaactc agcccttgcc tctgtatgac 420
acaccctatg agccagagga ggatggggcc accccggaag gtgagggggc cccctggccc 480
cgggagtcgc gcctgccaga ggatgatgag agggccctg aggagtatga mcagccctgg 540
gagtggaaga asgagcsgat ttccaaagcc tttgcagctg gtatcacggg gccatcagcc 600
gaaccgacgc cgagaacctg stccggctgt gcaaagagc cagytacytg gtgcgcaaca 660
gtgagaccag caagaatgac ttctccctct cctcaagag cagccaggga ttcatgcaca 720
tgaagctgtc ccgaaccaag gaacacaaat atgtgctggg ccagaacagc ccgcccctca 780
gcagcgtccc tgaaattgtg caccactatg ccagccgcaa gctaccatt aaggagccg 840
aacacatgtc cctgtcttac cctgtggcca tccgactct ttagatgtga agccagggca 900
ctgtgataga cctgtacca gccctgtgcc catcacctgg ctgagggctg tggctcttgc 960

cagggaacgt gaatctttca aacctttctt ctctgggna tccagtagaa gctggagatt 1020
ccttaattta ttctaaagg aaagggtcc tggggccttg gagtnaagg gttgtctgga 1080
gctggggaaa gaggaatccc tggagagaaa ggatagcccc tggaggaagg gggttccaga 1140
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gaattcggcc ccttggcggn ccttaccacc tctctgcctc cgtccccgay ttccaccca 1320
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tgggaagcag ccggtttttn ggggggttg ggagaggaag gggaggggtt cgggcaaagg 1440
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<210> 249

<211> 2301

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2297)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2298)

<223> n equals a,t,g, or c

<400> 249

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cgtgctcatg ctgccgtgac aacaggccac cacatacctc aacctgggga actgtatttt 120
taaataaga gctatttata tatattattt ttttttaaga aaggaggaaa agaaaccaa 180
agttttttt aagaaaaaaa atccttcaag ggagctgctt ggaagtggcc tccccagggtg 240
cctttggaga gaactgttgc gtgcttgagt ctgtgagcca gtgtctgcct ataggagggg 300
gagctgtag ggggtagacc tagccaagga gaagtgggag acgtttggct agcacccag 360
gaagatgtga gagggagcaa gcaaggtag caactgtgaa cagagaggtc gggatttgcc 420
ctggggagg aagagagcc aagttcagag ctctctgtct cccccagcca gacacctgca 480
tccctggctc ctctattact caggggcatt catgcctgga cttaacaat actatgttat 540
cttttcttt atttttctaa tgaggtcctg ggcagagagt gaaaaggcct ctctgattc 600
ctactgtcct aagctgctt tcttgaaatc atgacttgtt tctaattcta ccctcagggg 660
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gctagtgtg ctttgtgtgt atgtgtggca aataatttg gggtgatttg caatgaaatt 840
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ggaactccag gtcctttatt actgccttct tttcaaaagc acaactctc tctaaccctc 1020
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tcagtcactg tgcaatatgc ccctgggtc ccaggagggt ctggaggaaa actggctatc 1140
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gtttttctc cctggtgctc agagcacctg tgggaaagg ttgtgtctgt ctgagtacaa 1380
tccaaatttg tcgtarcttg tgcaatatat actgttgtg gttggagaaa agtggaaagc 1440
tacactggga agaaactccc ttccttcaat ttctcagtga cattgatgag ggtccctcaa 1500

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aagacctcga gtttcccaaa ccgaatcacc ttaagaagga cagggctagg gcatttggcc 1560
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cccaggttct cctccccaca gccagtcccc ttctctggat ttctaaactg ctcaattttg 1680
actcaaaggt gctattttacc aaacactctc cctacccatt cctgccagct ctgcctcctt 1740
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agttcacttt gggcccacag acccaagagc taattttctg gtttggtggg tgaaacaaag 1860
ctgtgaatca ctgcaggtg tgttcttgca tcttgtctgc aaacaggtcc ctgccttttt 1920
agaagcagcc tcatggtctc atgcttaatc ttgtctctct tctcttcttt atgatgttca 1980
ctttaaaaaac aacaaaaccc ctgagctgga ctgttgagca ggctgtctc tcctattaag 2040
taaaaaataaa tagtagtagt atgtttgtaa gctattctga cagaaaagac aaaggttact 2100
aattgtatga tagtgttttt atatggaaga atgtacagct tatggacaaa tgtacacctt 2160
tttgttactt taataaaaaat gtagtaggat aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2220
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2280
aaaaaaaaag gggggcnnc c 2301
```

<210> 250

<211> 2117

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (61)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (63)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (793)

<223> n equals a,t,g, or c

<400> 250

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nrnawgctcg ggccggcagg gtttccccgc acgctggcgc ccasmtcccg gcgcggagggc 120
crtgtaagtt tcgctttcca ttcagtggaa aacgaaagct gggcgggggtg ccacgagcgc 180
ggggccagac caaggcgggc ccggagcgga acttcggtcc cagctcggtc cccggctcag 240
tcccgacgtg gaactcagca gcggaggctg gacgcttgca tggcgcttga gagattccat 300
cgtgcctggc tcacataagc gcttcctgga agtgaagtcg tgctgtcctg aacgcggggc 360
aggcagctgc ggctggggg ttttgagtg atcacgaatg agcaaggcgt ttgggctcct 420
gaggcaaatc tgtcagtcca tcctggctga gtcctcgag tccccggcag atcttgaaga 480
aaagaaggaa gaagacagca acatgaagag agagcagccc agagagcgtc ccagggcctg 540
ggactaccct catggcctgg ttggtttaca caacattgga cagacctgct gccttaactc 600
cttgattcag gtgttcgtaa tgaatgtgga cttcaccagg atattgaaga ggatcacggg 660
gccaggggga gctgacgagc agaggagaag cgtcccttcc cagatgcttc tgctgtgga 720
gaagatgcag gacagccggc agaaagcagt gcggccctg gagctggcct actgcctgca 780
gaagtgaac gtngccctg tttgtccaac atgatgtgc ccaactgtac ctcaaactct 840
ggaacctgat taaggaccag atcactgatg tgcacttggg ggagagactg caggccctgt 900
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```

ataygatccg ggtgaaggac tccttgattt gcgttgactg tgccatggag agtagcagaa 960
acagcagcat gctcaccctc ccactttctc tttttgatgt ggactcaaag cccctgaaga 1020
cactggagga cgccctgcac tgcttcttcc agcccaggga gttatcaagc aaaagcaagt 1080
gcttctgtga gaactgtggg aagaagaccc gtgggaaaca ggtcttgaag ctgaccatt 1140
tgccccagac cctgacaatc cacctcatgc gattctccat caggaattca cagacgagaa 1200
agatctgcca ctccctgtac ttccccaga gcttgattt cagccagatc cttccaatga 1260
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agtgtacctc cggaaatcct aactaccact ggcaggaaac tgcatactt ctggtttaca 1500
tgaagatgga gtgctaattg aaatgcccaa aaccttcaga gattgacacg ctgtcatttt 1560
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gttttcaaac tatataactg agccttattt ataattaggg atattatcaa aatatgtaac 1680
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gccaaaggtc agtggcaggg ggtatttcag tattatacaa ctgctgtgac cagacttgta 1920
tactggctga atatcagtcg tgtttgtaat ttttactttt gagaaccaac attaatcca 1980
tatgaatcaa gtgttttgta actgctattc atttattcag caaatattta ttgatctct 2040
cttctccata agatagtgtg ataaacacag tcatgaataa agttattttc cacaaaaaaa 2100
aaaaaaaaa aactcga                                     2117

```

<210> 251

<211> 1446

<212> DNA

<213> Homo sapiens

<400> 251

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gccatcccc acaaaactcc ccctcaccaa agccgaggag aaggccttga agagagtccg 60
gaggaaaatc aagaacaaga tctcagccca ggagagccgt cgtaagaaga aggagtatgt 120
ggagtgtcta gaaaagaagg tggagacatt tacatctgag aacaatgaac tgtggaagaa 180
ggtggagacc ctggagaatg ccaacaggac cctgctccag cagctgcaga aactccagac 240
tctggtcacc aacaagatct ccagacctta caagatggcc gccacccaga ctgggacctg 300
cctcatgggt gcagccttgt gctttgttct ggtgctgggc tccctcgtgc cctgccttcc 360
cgagttctcc tccggctccc agactgtgaa ggaagacccc ctggccgcag acggcgtcta 420
cacggccagc cagatgcctc cccgaagcct cctattctac gatgacgggg caggcttatg 480
ggaagatggc cgcagacccc tgctgcccac ggagccccca gatggctggg aaatcaaccc 540
cggggggccg gcagagcagc ggcccsggga ccacctgcag catgatcacc tggacagcac 600
ccacgagacc accaagtacc tgagtggggc ctggcctaaa gacggtggaa acggcaccag 660
ccccgacttc tccactcca aggagtgktt ccacgacagg gatctgggccc ccaacaccac 720
catcaaaact tcctaggcca tgccaagacc caggacatag gacggacccc tggtagccag 780
aagaggagtt cttgctcact aaccgggatc cgcctcgtgc ccctgcctcc tggagcttcc 840
cattccagga gaaaaggctc cacttcccag cccttccctg cccctgaaca tttggactct 900
tcccttgggc cgaccactct gttctcattc tccttcccac caacatccat cgtccttct 960
cagacaaacc actcactggg taccacact cctctctcat atgcccaca cgaccactgc 1020
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ccttacccca cccccactgt acagagacca agaacagaaa ttgtttgtaa ataatgaacc 1140
ttatttttta ttattgcaa tcccctaaga tattgtattt tacaaatctc cctcttccct 1200
tcgccccctc cttgttttat attttatgaa gttagtgcgg gctttgctgc tccctggccc 1260
aggaaagagg gactacctga ccctcacctg gcacccccct gctgctgccc aagccgctgg 1320
gcctttttta ttgccaaact gctctcttca tcagctcagc acatgcttta agaaagcaaa 1380

```



```
accaaaaaaaaa aaaaaaaaaa gatgcagcat caaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1440
aaaaaa                                              1446
```

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<210> 252
<211> 2050
<212> DNA
<213> Homo sapiens
```

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<220>  
<221> misc feature  
<222> (596)  
<223> n equals a,t,g, or c
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<220>  
<221> misc feature  
<222> (1899)  
<223> n equals a,t,g, or c
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<220>  
<221> misc feature  
<222> (1922)  
<223> n equals a,t,g, or c
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<220>  
<221> misc feature  
<222> (1944)  
<223> n equals a,t,g, or c
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<220>  
<221> misc feature  
<222> (2012)  
<223> n equals a,t,g, or c
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<220>  
<221> misc feature  
<222> (2042)  
<223> n equals a,t,g, or c
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<400> 252							
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aggttatgct	gttgagtgat	gacgcatagc	tgcttttgct	ccatttyccc	cagatgactt	180	
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atgcattgtaa	gccagaagat	gtatgttact	ttgaaaacat	aagtaacaaa	attttgaatg	300	
tattgctaaa	gagatgtctc	tctgaagctc	ttttgatgtt	tggtgtcttg	tccttcctat	360	
taaaccatat	cttagtaaat	agtttggtac	gaatggattt	atcactgagc	aggctctgca	420	
aataattaat	cggtagcgtt	ttgtttctgt	tgatagaaat	aaaagagact	gatggaagct	480	
ctcagatcaa	gcaagaacca	gaccccacgt	ggtagacctc	ttccctccta	gggtaaatca	540	
gcttctgtgt	cagggatgct	gtgtggtgtc	catctgaacc	ccttgcatac	gcgtantaat	600	
gtgatctccc	cactttcaca	taagatggtg	gccctgcctt	cagggaaatg	gggagccaag	660	
tgqgaqcctt	cccqatattt	taagctagaa	gattctacag	ggagattctc	cttggatcaa	720	

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tatatgtctc tcagtcaaag atgtaaaagc acctttgcct taaaaagaat gttctgtttc 780
taaatagagt caacgttgtc ctcctcattg gaattcacta tgagtcagaa tcattagact 840
gacttttttt tttccatagt aatagtattt tgcagagtct cacagagctg cagatctttt 900
gttcatcttg cagagttaac aagtctgac ctgttagtcc agatttctta aatttggcca 960
agttataata ggagcagtag cttgagacc gaagtcagga aactttgaca atggattttt 1020
ttttttaatc cagagacttg tactggaatt tgccttacct tgtcagctca tggacttaag 1080
gtttcatccc gctttatgag tgcttctgaa tccaagtcac tgttacctga atttgcaaat 1140
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gtttgttttc tctccctatt ttagccttaa agtatccagt ggttgaagaa agagcttttc 1260
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tcctacttct cctactggaa catctcagct tctgcagtga agaaaaattc ctgtgatagt 1620
tcagttcttt agtttttcta ttgaaaaaa aaaaatcatt taaatgatcc ttgtttcacg 1680
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cycttcact tttacttttc gtcccaaata aaatgcatng gtgtaccaga agttgaagat 1920
cnggggtgar gattggggct agcncgatga cactwaggcc ccmacatcgc gggamctgct 1980
gtggcgcgga ttcttaggac gctgttttag cngggcccct ctccaagggc gccgtgggcy 2040
gnaatatcc 2050
```

<210> 253

<211> 2529

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2523)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2529)

<223> n equals a,t,g, or c

<400> 253

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aaggactgcc agaaaacatt cttttccgaa gtccctcatg gtatggaatc ccaaggctgg 180
aaaaaatcat tcaagtgggc aatcgaatta aatttggtat taaaagacca gaacttctga 240
ctcacagtac cactgaagtt actcagccaa gaacgaatac accagtcaaa gaagattgga 300
atgtcagaat taccaagcta cggaagcaag tggaagagat ttttaatttg aaatttgctc 360
aagctcttgg actcaccgag gcagtaaaag taccatatcc tgtgtttgaa tcaaaccggg 420
agttcttgta tgtggaaggc ttgccagagg ggattccctt ccgaagccct acctggtttg 480
gaattccacg acttgaaagg atcgccrcg ggagtaataa aatcaagttc gttgttaaaa 540
aacctgaact agttatttcc tacttgctc ctgggatggc tagtaaaata aacactaaa 600
ctttgcagtc ccccaaaaaga ccacgaagtc ctgggagtaa ttcaaagggt cctgaaattg 660
```

```

aggtcaccgt ggaaggccct aataacaaca atcctcaaac ctcagctgtt cgaacccccga 720
cccagactaa cgttcttaac gttcccttca agccacgagg gagagagttt tcctttgagg 780
cctggaatgc caaaatcacg gacctaaaac agaaagttga aaatctcttc aatgagaaat 840
gtgggggaagc tcttggcctt aaacaagctg tgaagggtgcc gttcgcgtta tttgagtctt 900
tccccgaaga cttttatgtg gaaggcttac ctgagggtgt gccattccga agaccatcga 960
cttttggcatt tccgaggctg gagaagatac tcagaaacaa agccaaaatt aagttcatca 1020
ttaaaaagcc cgaatggtt gagacggcga ttaaggagag cacctcctct aagagccctc 1080
ccagaaaaat aaattcatca cccaatgtta atactactgc atcagggtgt gaagacctta 1140
acatcattca ggtgacaatt ccagatgatg ataatgaaag actctcgaaa gttgaaaaag 1200
ctagacagct aagagaacaa gtgaatgacc tctttagtcg gaaatttggg gaagctattg 1260
gtattgggtt tcctgtgaaa gttccctaca ggaaatcac aattaaccct ggctgtgtgg 1320
tggttgatgg catgcccccg ggggtgtcct tcaaagcccc cagctacctg gaaatcagct 1380
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aagaatcagc tgaaccaagc cagttggaag ttccagccac agaagaaata aaagagactg 1560
atggaagctc tcagatcaag caagaaccag accccacgtg gtagacctct tccctcctag 1620
gccttgagtt acggtgttta ttttccaatc aagtgaagat atctcctact tctcctactg 1680
gaacatctca gcttctgcag tgaagaaaaa ttctgtgat agttcagttc tttagttttt 1740
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cctatgtttt tttatcataa ttaaaagcaa aaccatctgg atcacctaac agtcagaggt 1920
cagtatctca gcgtgtgaat tatagaggaa atacagagag aacctcttcc acttttactt 1980
ttcgtccaaa taaaatgcat ggtgtaccag aagttgaaga tcgggttgag gattggggct 2040
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cgctgttcta gccggccccc tctccagggg tcgccgtggc cggcattatt tcctagttct 2160
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tgcgagttgt aaaataccag ctctacaaga agctaggctc tgtgacggca tagttttcag 2340
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tttatgtgtt gcttctatct tacctcaaat tgtagatata gggtaatcaa taaaatccat 2460
ccatgccttt cacacactaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2520
aangggggn
2529

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<210> 254

<211> 1678

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1676)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1678)

<223> n equals a,t,g, or c

<400> 254

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ggccacgggg acgccgtgtg gggcctggcc ttcagtccca cctcccagcg cctggcctcc 180
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<210> 255

<211> 966

<212> DNA

<213> Homo sapiens

<400> 255

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agttagcttg tagtgacaaa aacaaaggagg aaaaaaagaa gagaactgtc tgaggaacag 180
aaacaagaaa ttaaagatgc ttttgaacta tttgatacag acaaagatga agcaatagat 240
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ctgaagattc ttaaagatta tgacagagaa gccacaggga aaatcacctt tgaagatttt 360
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aaaaaa 966

<210> 256
<211> 3091
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (3040)
<223> n equals a,t,g, or c

<400> 256
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tgaagaactg cattggaaaa gaactctcta agatcccat gccggtaaac tttaatgagc 180
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cattgtatctt tccatgcaac tgggcaccac tacacttgga agaaagttac cacaactgta 600
cacaacatta ttgtgggcaa gttgtggata gatcagctctg gcgaaattga tattgtgaat 660
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cctagttgtg ataaacatgg gagaggagtg a 3091

<210> 257

<211> 2952

<212> DNA

<213> Homo sapiens

<400> 257

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aaacaggagc ctacatgta tcgagagggg ccccttacc agaggcgagg ttcccttcag 180
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atccagaaga accggccagc catgaactat gacaagctga gccgctctct ccgtattac 360
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aaaaaaaaaa aa 2952

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<210> 258

<211> 2217

<212> DNA

<213> Homo sapiens

<400> 258

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ctactgggca aatacactta ctgtgttcta gaggcagccc tttcttatgc agaaaaataca 180
atacgcactg catgagaagc ttgagagtgg attctaatacc aggtctgtcg accttgata 240
tcatgcatgt gggaagggtg gtgtggtgag aaaagtttta aggaagagt agatggccat 300
gttcaacttt acaaaatttc ttggaaaact ggcagtattt tgaactgcat cttctttggt 360
accggaacct gcagaaacag tgtgagaaat taagtcctgg ttcactgcgc agtagcaaag 420
atggtcaagg ccatggaaaa agcagaaatt taccaagaaa gctgataccc atgtatagtt 480
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caaactttta ttttgttaaa tttatatggc tttgaaatag aagtataagt tgctaccatt 720
ttttgataac attgaaagat agtattttac catctttaat catcttgga aatacaagtc 780
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aatgaatgct tagaagctgt tcacatcttc aagagcagaa gcaaaccaca tgtctcagct 1560

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ggttttaccc tctattttaa tgctttgaaa aacagtgcac tgacaatggg ttgatatttt 1680
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<210> 259

<211> 1240

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1240)

<223> n equals a,t,g, or c

<400> 259

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atccccgctg acccgatcaa cctgtacgcc aacgccgccg acatcgacta tatagcaggc 120
accaacaaca tggacggcca catcttcgcc agcatcgaca tgccctgccat caacaagggc 180
aacaagaaag tcacggagga ggacttctac aagctggtca gtgagttcac aatcaccaag 240
gggctcagag gcgccaagac gacctttgat gtctacacyg agtcctgggc ccaggacceca 300
tcccaggaga ataagaagaa gactgtggtg gactttgaga ccgatgtcct cttcctggtg 360
cccaccgaga ttgccctagc ccagcacaga gccaatgcc aagatgccaa gacctacgcc 420
tacctgtttt cccatccctc tcggatgccc gtctacccca aatgggtggg ggcggaccat 480
gcagatgaca ttcagtacgt tttcgggaag cccttcgcca cccccacggg ctaccggccc 540
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gacccaaca tgggcgactc ggctgtgccc acacactggg aaccctacac tacggaaaac 660
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cgtcccatga gccttggtat caagaggcca caagagtggg accccagggg ctcccctccc 1140
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aaaaaaaaa aaaaaaaaaa aaaaaaaggg gggggggccn 1240
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<210> 260

<211> 610

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (559)

<223> n equals a,t,g, or c

<400> 260

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gctctatgac aagagcgacc cctactatga gaactgctgc gggggcgccg agctgtcgct 180
ggagtccggc gcagacctgc cctacctgcc ctccaactgg gccaacaccg cctcctcact 240
tgtgtggcc ccgcgctgcg agctcaccgt gtggtcccg caaggcaagg cgggcaagac 300
gcacaagttc tctgccggca cctacccgcg cctggaggag taccgccggg gcattctagg 360
agactggtcc aacgctatct ccgcgtcta ctgcagggtgc agctgatgca ttgctggtct 420
ctcatctgca gcttccacag agtgccaagc cctcactca gccatccct gggctctgct 480
ccggggcccc aagaccagc aggaggagcg ttctgcctgc ccctccac ctyccctgca 540
atacaagcct ttgtgcagnt gtaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600
aaggcgcc 610
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<210> 261

<211> 2116

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (7)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (16)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (25)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (35)

<223> n equals a,t,g, or c

<400> 261

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ccggaattcc cgggtcgacc cagcgctccg aaatgaatag atgggccagc tggaaagggt 120
accacagct aagggccatc ttattgaacc cccaagaagt caaatgtagt catccctaac 180
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caaccacagg gcacttgtgc gcgcgcacac acacacacac acacaaatat gcaaatactc 240
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<211> 1557

<212> DNA

<213> Homo sapiens

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<222> (1347)

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<400> 262

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<211> 1654

<212> DNA

<213> Homo sapiens

<400> 263

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ctctttatca ggatatggaa cagatgctat catctactta aaggctttgt cttctgagtc 180
tatagaaaaa ctccagttt ttaacaagtc agccttcaaa cattatcaga tgagctctga 240
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<210> 264

<211> 1168

<212> DNA

<213> Homo sapiens

<400> 264

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<211> 1757
<212> DNA
<213> Homo sapiens

<400> 265
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<211> 414
<212> DNA
<213> Homo sapiens

<400> 266
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<210> 267
<211> 1452
<212> DNA
<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<211> 764

<212> DNA

<213> Homo sapiens

<220>

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 <222> (625)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (739)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (747)
 <223> n equals a,t,g, or c

<400> 269
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 ggaggccaag acgctggtgc acacgctgga cggctggtcc gtggtgcaga caatggtcgt 180
 gtccacaaaa acgccggaca ggaagctcat ctttgcaaa gggaactttg agcacctgac 240
 agaaaagatc cgagggtctc cagacgtcac gtgcgtcttc ctgaacgtgg agaggatggc 300
 tgccccgacc aagaaagaac tggaagccgc ctggggcktg gagtggtttg accgcttcac 360
 ggtcgctcctg cacatcttcc gctgtaacgc ccgcacgaag gagggccggc ttcagggtggc 420
 cctggcggag atgccgctgc acaggctcga cttgaaaagg gacgtcgccc acctgtaccg 480
 aggagtcggc tcgcgctaca tcatggggtc aggagaatcc ttcatgcagc tgcagcagcg 540
 tctcctgaga gagaaggagg cyaagatcag gaaggccttg gacaggcttc gcaagaagag 600
 gcacctgctc cgccggcagc gacgnaggcg ggagttcccc gtgatytccg tgggtggggta 660
 caccaacttg cggaaagacc acgtgatcaa ggattgacgg ggcgatgccg ccattccagc 720
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<210> 270
 <211> 532
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (467)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (513)
 <223> n equals a,t,g, or c

<400> 270
 ggcagagccc ccacctgcca gagctgatcc tccctaggcc ctgcctaacc ttgagttggc 60
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 atcttttgag agctgagggg tgagggcatt gagccaacac acagatttgt cgcctctgtc 180
 cccgaagaca cctgcaccct ccattgcggrc caagatgggg aatggaactg aggaagatta 240
 taactttgtc ttcaagggtg ctatcggtgt gcagtggggg ccctcctggt gtttgacctg 300
 accaagcacc agacctatgc tgtggtggag cgatggctga aggagctcta tgaccatgyt 360


```

gaagccacga tcgtcgatcat gctcgtgggt aacaaaatga cctyagccag gcccggaag 420
tgcccatgag gagggccgaa ttctgttgaa aacaatggat gttttcntga gactcagcct 480
ggatttacca tgttgagtag ctttgagatt tcngaagaaa ttttgcgagt tt 532

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<210> 271

<211> 1397

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (109)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1242)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1378)

<223> n equals a,t,g, or c

<400> 271

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naaaccgagt tattcatcga gacctcaagc tgggcaacct tttcctgaat gaagatctgg 60
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agacccatgt gtgggactcc taattacata gctcccagg tgctgagcaa gaaagggcac 180
agtttcgagg tggatgtgtg gtccattggg tgtatcatgt atacctgtt agtgggcaaa 240
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gatcccaactg cccgcccac cattaacgag ctgcttaatg acgagttctt tacttctggc 420
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cccagcagcc tggacccag caaccggaag cccctcacag tcctcaataa aggcttggag 540
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gtggtcgact gccacctcag tgacatgctg cagcagctgc acagtgtcaa tgcctccaag 660
ccctcggagc gtgggctggg caggcaagag gaggctgagg atcctgcctg catccccatc 720
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gataacagcg tggggggtgc tcttcaatga ctcaacacgc ctcatcctct acaatgatgg 840
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cagcgtgacg atcaacttct tccaggatca caccaagctc atcttggtgc cactgatggc 1140
agccgtgacc tacatcgacg agaagcggga cttccgcaca taccgcctga gtctcctgga 1200
ggagtacggc tgctgcaagg agctggccag ccggctccgc tnacgcccgc actatggtgg 1260

```

acaagctgct tgagctcacg ctcgccagc aaccgtytta aggcctccta attagttgsc 1320
cttcccttcc ggaattggtg gccttcttca tttcccaatt ggcattttgg ggggccnaa 1380
ttggtttggg ttcccg 1397

<210> 272
<211> 527
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (413)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (501)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (507)
<223> n equals a,t,g, or c

<400> 272
ggttgagctg ctgccgcgc cgctctgtc gtcgtcgcga gtgtggagtc gggactggag 60
ctgctgccgc ggcgacgccg gggatctttg tcgctagctc ccggcccttc tgccccgccg 120
ccttccctca gtcagcggtg cccactcctc tccggccggg cgccctgcc tccatttctc 180
gctctctgtc caccacacac acggcccccc cgatcatgga tccgggcagt ggcggcggcg 240
gcggcggcgg gcggcggcgc gggagcagca gcggcagcag cagcagcgac tcggcgccctg 300
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ccctggcggc ggcggccgag gccagcggg agaacctcag cgcgcccttc agncggcaac 420
tcaacgtcaa cgccaagccc ttcgtgccca acgtccacgc cgccgagttc gtgccgtcct 480
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<210> 273
<211> 805
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (5)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (792)
<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (794)

<223> n equals a,t,g, or c

<400> 273

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cccgggccag ggctgcccct aatctctgta ggaaccgtgg tatgtctgcc atgttgcccc 120
tttctctttt cccctttcct gtcccaccat acgagcacct ccagcctgaa cagaagctct 180
tactctttcc tatttcagtg ttacctgtgt gcttggtctg tttgacttta cgcccatctc 240
aggacacttc cgtagactgt ttaggttccc ctgtcaaata tcagttaccc actcgggtccc 300
agttttgttg cccagaaaag ggatgttatt atccttgggg gctcccaggg caaggggttaa 360
ggcctgaatc atgagcctgc tggaagccca gccctactg ctgtgaaccc tggggcctga 420
ctgctcagaa cttgctgctg tcttggtgcg gatggatgga aggttggtg gatgggtgga 480
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tgttgagcat gacagcctgc agcaggaata tatgtgtgcc tatttggtg gacaaaaata 600
tttacctta gggtttgag ctattcaaga ggaaatgtca cagaagcasc taaaccaagg 660
actgagcacc ctctggattc tgaatctcaa gatgggggca gggctgtgct tgaaggccct 720
gctgagtcac ctgttagggc cttggttcaa taaagcactg agcaagttga raaaaaaaaa 780
aaaaaaaaaa ananaaaaaa aaagg                                     805
```

<210> 274

<211> 1953

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (196)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (522)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (524)

<223> n equals a,t,g, or c

<400> 274

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gctgcccggc gagctggcca agcacgccgt gtccgagggc accaaggcgg tcacccaagt 120
acaccagct ccaaagttkg aactgccggg acctggcgct cgctcgctcg agtcgccggc 180
tgcttgactc caaaangetc ttttcagagc caccaccta atcactagaa aagagcttgt 240
tcacttattc cttagtttc ttttcataaa gtaagttatt ttagtgtgaa ggtcatggga 300
aatggcatag gtagcttttt aactatttgg aactcgaggt cccagtgcg tcattggatt 360
tgcttttgaa tctagagcgt gtctttactc attgtgctgc ttagccttcc caggagtcgg 420
ttctcaatta ggctgttggg aatccgcctc ttaccgcc ccactccc cccacacgc 480
gccctggtgg ctcccttgggt ctgtttcatt ctaaaacgaa gngnctgagt tgggctgtca 540
tttaagagaa ctccaggaca caattcagcc cgggttccgc aaacactgcg tgacagctct 600
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gccttgtcct gattgggcga caagaatatt caaaattctg cgccttttct taattttag 780
atttcagttt ccgctcgttca ctttgagact ttgaaattcc tatttctcat tttgttgata 840
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tcttaactgt ctctacatg tgtgttttca aatgtgtata gatgctattg ttattaataa 1920
agttaccaat taatttaaaa aaaaaaaaaa aaa 1953

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<210> 275

<211> 2376

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (86)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (275)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1965)

<223> n equals a,t,g, or c

<400> 275

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gcagctctct gcctctctgc cctttggtct rtgttcacag gtgacccgtg tcagcctgca 420
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aataagattc agctggtcag acttttctgg gcagtctcag tgacgcattt cctgtgctgt 2280
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<210> 276

<211> 2439

<212> DNA

<213> Homo sapiens

<400> 276

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acatggaggc tttaacaaga cttcacatta ctgtttctaa agcctacaaa gttaacccag 360
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aactccatct tagcttttat ctgactagta tctatgacca ttcaatattt gaagccttta 540
gtaagggtgt gcagaaactc attccacaac tgccgacctt ggaaaacctt ttaaatatct 600

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ttatatcaaa ttcaggtatt gaaaaagctt ttctctttga tgttgtcagc aaaatctaca 660
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<210> 277

<211> 1889

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1076)

<223> n equals a,t,g, or c

<400> 277

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gtgtgccaca acgggggtgct aggcctgagc cgctgtgtgt ttttctgct gggcttctc 360
cggattcgcg ttcgtggcca gcgagcctct cgcttcaag cccctgtcct tgttgctgcc 420
ccacactcca ctttctttga cccattgtt ctgctgccct gtgacctgcc caaagttgtg 480

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```

tcccagagctg agaacctttc cgttcctgtc attggagccc ttcttcgatt caaccaagcc 540
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<210> 278

<211> 636

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (608)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (632)

<223> n equals a,t,g, or c

<400> 278

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636

<210> 279

<211> 2861

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2861)

<223> n equals a,t,g, or c

<400> 279

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<210> 280

<211> 1506

<212> DNA

<213> Homo sapiens

<400> 280

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tgtacaccca agccgtgcaa aacattcggg ttgttggggc ggagacagct ttcttaatac 480
aagcactgtc gacgcagctg gggtagagcc ttgaggacgt gcatgtcatc ggccacagcc 540
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aaaaag 1506

<210> 281

<211> 1693

<212> DNA

<213> Homo sapiens

<400> 281

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<210> 282

<211> 1223

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1159)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1196)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1208)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1223)

<223> n equals a,t,g, or c

<400> 282

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acaagggcga tgtggccatg agcaagattg agcacttcat gcctttgctg gtacagcggg 180
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<210> 283

<211> 490

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (57)

<223> n equals a,t,g, or c

<400> 283

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gggtgattgg agattattag attctagggt aacttctacc actttaccct aatacataaa 180
actttttcct aaataaatga tggaaggaaat aatacttggg tacctggcat tatttttcag 240
taagaaaaaa gctttactaa ccactacatt tatggaaatt tgtaggggta agtattttat 300
aggtcataaa aaacaccata atataacgaa tctcattttc tttaaatgtg aattaaatcc 360
taacagtcac ttttataaaa tgaccatagg ctaaaatctt acgtgtaagt actactacaa 420
taaataattt ctgaaacctt taaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480
gggggggggc 490
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<210> 284

<211> 3009

<212> DNA

<213> Homo sapiens

<220>
<221> misc feature
<222> (412)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (548)
<223> n equals a,t,g, or c

<400> 284
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<210> 285

<211> 876

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (740)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (760)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (813)

<223> n equals a,t,g, or c

<400> 285

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agccctacaa atgtgaggtc tgcagcaagg cttctccca gagctctgac ctcatcaaac 180
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gcccttcaag tgccctgagt gcggcaagcg ctttggccag agctcgggtg tggccatcca 600
cgcccgacac cacttgccag gycgcacctc cagctgcccc gactcgggca agaccttcaa 660
tcgctcctcc actctcatcc agcaccagcg ctcccacacg ggcgagcggg ccctgacagg 720
tggcgcggtg tgcgcagagn gggtttctg ccgtgcctn ccacgcttcc tggcagcatt 780
caccgggttc cagcgtgggc ggagcgggcc ttnacaagtg gcgatggatt gcgggaaagg 840
cctttcttcc cagagcttcc ggaccttcat tccggc 876

```

<210> 286

<211> 861

<212> DNA

<213> Homo sapiens

<400> 286

```
gacacctctg tcaccatgtg gttcctgggt ctgtgcctcg ccctgtccct gggggggact 60
ggtgctgcgc ccccgattca gtcccggatt gtgggagggt gggagtgtga gcagcattcc 120
cagccctggc agggcgctct gtaccatttc agcactttcc agtgtggggg catcctgggt 180
caccgccagt ggggtgtcac agctgtcat tgcatcagcg acaattacca gctctggctg 240
ggtcgccaca acttgtttga cgacgaaaac acagcccagt ttgttcatgt cagtgaagac 300
ttccacaccc ctggcttcaa catgagcctc ctggagaacc acaccgcca agcagacgag 360
gactacagcc acgacctcat gctgtccgc ctgacagagc ctgctgatac catcacagac 420
gctgtgaagg tcgtggagtt gccacccag gaaccggaag tggggagcac ctgtttggct 480
tccggctggg gcagcatcga accagagaat ttctcatttc cagatgatct ccagtgtgtg 540
gacctcaaaa tcctgcctaa tgatgagtg raaaaagccc acgtccagaa ggtgacagac 600
ttcatgctgt gtgtcgaca cctggaagg ggcaaagaca cctgtgtggg tgattcaggg 660
ggcccgctga tgtgtgatgg tgtgtccaa ggtgtcacat catggggcta cgtcccttgt 720
ggcaccacca ataagccttc tgtcgccgtc agagtgtgt cttatgtgaa gtggatcgag 780
gacaccatag cggagaactc ctgaacgccc agccctgtcc cctaccccca gtaaaatcaa 840
atgtgcatcc aaaaaaaaaa a                                     861
```

<210> 287

<211> 1068

<212> DNA

<213> Homo sapiens

<400> 287

```
aattcggcac gaggtcactg ctggctgaag gctgcgctca ggcccgtgga tctcatcgaa 60
gatggcggcg cgatctgtgt cgggcattac cagaagagtc ttcatgtgga cagtctcagg 120
gacaccatgt agagaathtt ggtctcgatt cagaaaagag aaagagccag tggttgttga 180
gacagtagaa gagaaaaagg aacctatcct agtgtgtcca cttttacgaa gccgagcata 240
cacaccacct gaagatctcc agagtctgtt ggaatcttac gttaaagaag tttttgggtc 300
atctcttctt agtaattggc aagacatctc cctggaagat agtcgtctaa agttcaatct 360
tctggctcat ttgctgatg acttgggtca tgtagtcctt aactccagac tccaccagat 420
gtgcagggtt agagatgttc ttgatttcta taatgtccct attcaagata gatctaaatt 480
tgatgaactc agtgccagta atctgcccc caatttgaaa atcacttggg gttactaagc 540
aattcggaag agaaacacat tgaaatcact gtctttccct gagcaagggg gctgctcatt 600
agatcttttg atactttacc atgtgaaata ctaccagaac tgttctctaa acccactttt 660
tctgtagagg aatgtatcat cttttttttt ctcatattac aaatggacaa ataacggact 720
ttctattttc atatttgctg aaaccatttt ttaaataaaa ttaggtcatt atttatgaaa 780
agttttgaga gggcactgtc aacttgggtt taagacagga ggacattgca agttcacacc 840
tttcataagc ataaagtagt tgcaagaaag tattttcatt ctgttaggat tcataatctaa 900
gatagagtta tgcatgtcac atacacaaat aaacttttat tagatagata cctataaaaag 960
aaacataaaa gtatgttgtg tattactgac agttctagat taatttcttt tagaattaaa 1020
gtagatttgt taaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1068
```

<210> 288

<211> 2256

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (42)

<223> n equals a,t,g, or c

<400> 288

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tgtgcttggg gaatctaccc ccaacccaaa cccaggctgt cnatcgcccc tcaacccttc 60
ttccaaacta cgtgctgaag ccgttcttcc ccaacctgtt tccccccca gagtcctggg 120
tcggctcctg gctgccaatc tgcttattgc tcctcacatg ggtcaactgt tccagtgtgc 180
gggtgggccac ccgggttcaa gacatcttca cagctgggaa gtcctggcc ttggccctga 240
ttatcatcat ggggattgta cagatatgca aaggagagta cttctggctg gagccaaaga 300
atgcatttga gaatttccag gaacctgaca tcggcctcgt cgcactggct ttccttcagg 360
gctcctttgc ctatggaggc tggaaacttc tgaattacgt gactgaggag cttgttgatc 420
cctacaagaa ccttcccaga gccatcttca tctccatccc actggtcaca tttgtgtatg 480
tctttgccaa tgcgcttat gtcactgcaa tgteccccc ggagctgctg gcatcmaacg 540
ccgtcgctgt gacttttggg gagaagctcc taggagtcac ggcttgatc atgcccattt 600
ctgttgccct gtccacattt ggaggagtta atgggtctct cttcacctcc tctcggtgtg 660
tcttcgctgg agcccgagag ggccaccttc ccagtgtgtt ggccatgatc cacgtgaagc 720
gctgcacccc aatcccagcc ctgctcttca catgcatctc caccctgctg atgctgggtca 780
ccagcgacat gtacacactc atcaactacg tgggcttcat caactacctc ttctatgggg 840
tcacggttgc tggacagata gtccctcgct ggaagaagcc tgatatcccc cgccccatca 900
agatcaacct gctgttcccc atcatctact tgctgttctg ggcttctctg ctggtcttca 960
gcctgtgggc agagccgggtg gtgtgtggca ttggcctggc catcatgctg acaggagtgc 1020
ctgtctatct cctgggtgtt tactggcaac acaagcccaa gtgtttcagt gacttcattg 1080
agctgctaac cctggtgagc cagaagatgt gtgtggctgt gtaccccgag gtggagcggg 1140
gctcagggac agaggaggct aatgaggaca tggaggagca gcagcagccc atgtaccaac 1200
ccactcccac gaaggacaag gacgtggcgg ggcagcccca gccctgagga ccaccattcc 1260
ctgggtactc tctccttctc ccccttttta tctacctcc ctgccttggg cccgccaaca 1320
catgcgagta cacacacacc cctctctctg cttttgtcag gcagtggtag gactttgggtg 1380
tgggtgggtg gaaattgtaa acaaaaactg acattcatac ccaaagaacc agcctctcac 1440
cccagggtcc atgtcccagg cccactcca gtgctgcccc cactcccagc tgctggagga 1500
gaggggagat gccaaagtgc cctgcaggac ctccctccgg gccacacctc cagctgcctc 1560
ttcaggaacc ggagctcatt actgccttcc ctcccaggga ggcccttca gagaggagag 1620
gccacaggag ctgcattgtg gggggacagg ctcaagcaat tctgtcccca tcaaggggtc 1680
agctggagag acccaagacc ctatctgttc accagggacc caaaatccaa ggggatgctt 1740
ccctctgccc tctttctctg ccttcccat catacctgca cccaccccag ccagggtctc 1800
ctgtccagaa ttcggttctc ctcaggacgc caactcccag agctaaggac caaggagaag 1860
aacagcctct ccaccccaa gccaggcggg tgaggaaacat attgagaaag gttcagattg 1920
cagaaaccca gccctgcccc tgccctctgc atccagcccc caacatgggtg ccaaagcttc 1980
cagaagccaa aaagcttctg atttttaagg tagtgggcat ctctctccta atgacgaagc 2040
tgctcagcaa ctccacctgc ccgcgcagg aaggagcagt cccctgctat cctgcagcc 2100
actcccagca caccgcaca cagccagcac caccgtcccc accgtgcaact tctyctctct 2160
gggccttggg ttggggacca gggtagggag ggattcccca aggcctttca gggcttgagg 2220
ttcagaggcc agattcagct ttaagggtta cttcca 2256
```

<210> 289

<211> 331

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature
<222> (273)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (279)
<223> n equals a,t,g, or c

<400> 289
agtatctatc ccaaggattt tagcatttat cccaagagca tttatccaag agcatttattc 60
ccaaaagtat ttatcccgat gatttttagca tttatccgaa gagtatttat cccaaggata 120
gcattttatcc caagagcatt tacccaagag catttttccc aagactattt atcccaaaga 180
tttttagcatt tatcccaaga gcattttacc aagagcattt atcccaagga attttgtttt 240
gttttgtttt gtgtttttga gacagagtct ttntctgtna cccaggctgg agtgagccga 300
gatcgtgccc actgcacttc cagtctgggc g 331

<210> 290
<211> 705
<212> DNA
<213> Homo sapiens

<400> 290
aatatcacca aactgattgt aaatgtgcgg ctgtagcaga catttttagtg tgggtggtgtg 60
cagccatttc ggccctacac ctgccagcct ggctacctta cagttgtgtt ccgatttttg 120
cgtctatgct tgggtgtgcct cacttgctgc attttccagc atgcaaccag gagttgacgt 180
aggaaaaagg gatgctttct tactttggaa gctctcaggg aagttggtgt caatttctcc 240
tccactgcct ggccctaccct gcaactccaa agattttgtg cagatgggta gttccatttt 300
ttaaaaattg tgcagatatg gaaaattgtg acttacttca tgaccagaac tatctagaat 360
atgtgtggtg gtataaacat cttgcttaac caaatatcta ttaggcaga ggtaaccagg 420
agagaagcaa gacttgctgc cttaaaggagc ccaccatttt acttttcaca ttaaatctgc 480
cacgttgaat caattggaat aaaacctgac tcgcaggtga ctggacagga aatcccaaag 540
ttccaccatt tctatgctta attttaacgt ccccccgtt tttttttgt agaaaataaa 600
aacaagaaaa tcgttccaat gtaagatgtt tgttatagaa actttaggca atacaggtgt 660
gtaataaaat gtttaataaa cttctaaaca cttttgtatt tggat 705

<210> 291
<211> 952
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (827)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (943)
<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (948)

<223> n equals a,t,g, or c

<400> 291

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aaggctaattg aaattgcatt ccaggtaggg gttaacgtca aatttccatg gctggtagct 60
gtgcttttgg catatcacag tgttgtgtca ctactacaag gtaaagcatc tacagcggag 120
aatgagcttg aaaatgagag acctattgwg aataaatatg cccatgagag catatttaat 180
aagcctctat aacatgcagc caaaccagac attcactcct gcagagaaat gttgccctgg 240
agaaaaagaa atatataaag ataggctatc acccttcttt tgctgcagta ctaagcatag 300
caagaaatta gaatcattta cattggaaat ttgaaaatc cctttatata cacaacttta 360
ctgtgtataa ataaaaaata tttattaatg cagtgtatgc cgtcagttgt tttaggaatg 420
gcttctgcaa ttagaaaaat agcttgctag aatgtaaaatg ttctgttact ggtaaatgta 480
ctgcacacat tcattggacg ttaaaacaag tgagtagcct tttttacctg ccagcagcat 540
ggctgtgtgc agccactagg ctgaggacaa taaattacca aaaattataa tgtaccgagc 600
tgaaaatgct cagtacatta tgtggcata tctggatgtg atgagaaatc tcattgccat 660
ttgggacact gacatcccag aagtaatcca caactgcttt gcaaaagcaa agtgactgct 720
cagatgaaca gagcagagta ctactcact atgggtggcat cagctgcaaa gcgaaaatga 780
actgtcccat gatcatgttg atggttttct agatactgcc aacatgntta ggctcttttc 840
tggatgctga tggagttttc aaacacggaa cagacaccct tgatgtgggg ttttgctaag 900
gaacatrgga ggaacgggag gaaagtgtgc ccgggttcac acntcccngg gg 952
```

<210> 292

<211> 604

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (557)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (580)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (582)

<223> n equals a,t,g, or c

<400> 292

```
ggcagagtga aagaaggatg tktttgcttc tccttctgcc atgattgtaa cattcccaga 60
acctggaggc caggctatga cacagagtca atcaataacc agggagatct gtgaatatag 120
cccagtaggt ggggccttgc tgccatctgc catatgacct ttccagtccc aggccttctga 180
agagacgtgg taagtgcggg gcagttttca actgacctct ggacgcagaa cttcagccat 240
gaaggtaaca ggcattcttc ttctcagtgc cttggccctg ttgagtctat ctggtaacac 300
tggagctgac tccctgggaa gagaggccaa atgttacaat gaacttaatg gatgcaccaa 360
gatatatgac cctgtctgtg ggactgatgg aaatacttat cccaatgaat gcgtgttatg 420
```

```

ttttgaaaat cggaacgcc agacttctat cctcattcaa aaatctgggc cttgctgaga 480
accaagggtt tgaaatccca tcaggtcacc gcgaggcctg actggcctta ttgttgaata 540
aatgtatctg aatatcnaaa aaaaaaaaaa aggcggccgn tntaaaagga tccagcttta 600
cgta 604

```

```

<210> 293
<211> 510
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc feature
<222> (480)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (491)
<223> n equals a,t,g, or c

```

```

<220>
<221> misc feature
<222> (508)
<223> n equals a,t,g, or c

```

```

<400> 293
gtgtcccca actcctggag tttccaccc tgagctgta aaaacctgcc ctgcctgtca 60
cccatttctg tgccaccagc ccacccctg cctccactct cctccctgcc accttctgtc 120
cctgccatag gaatatgggg acaccgtgta caccattgaa gttccctttc acggcaagac 180
gtttatcctg aaggtgagtg aggggagcgg gtgtcctgga gccccagaca gcacaggagg 240
ctccaggaag gtgccgaggg gccctctggt ggggtgcccc caccaagagg gaagggttg 300
tctgcccgag cccatctggc accacccagc cctctgccgc cctgtcccag accttctgc 360
cctgtcctgc ggagctcgtg taccaggagg tgatcctgca gcccagagg atkgtkctkt 420
ggaaaagaca gtgactgcct gccagatcct gcagcgagtg gaagacaaca ccctcatctn 480
ctatgacgtg nctgcagggg cttgcggncg 510

```

```

<210> 294
<211> 845
<212> DNA
<213> Homo sapiens

```

```

<400> 294
aattcggcag agctgacctg acaagccacc tcaagtggac aaggcactta ccaacagaga 60
ttgctgattt gtcctttaag caagagattc actgccgcta agcatggctc agaccaactc 120
gttcttcatg ctgatctcct cctgatgtt cctgtctctg agccaaggcc aggagtccca 180
gacagagctg cctaattccc gaatcagctg ccagaaggc accaatgcct atcgctccta 240
ctgctactac tttaatgaag accctgagac ctgggttgat gcagatctct attgccagaa 300
catgaattca ggcaacctgg tgtctgtgct caccagggcg gagggtgctc tcgtggcctc 360
actgattaag gagagtagca ctgatgacag caatgtctgg attggcctcc atgacccaaa 420
aaagaaccgc cgctggcact ggagtagtgg gtccctggtc tcctacaagt cctgggacac 480
tggatccccg agcagtgcta atgctggcta ctgtgcaagc ctgacttcat gctcaggatt 540

```

```

caagaaatgg aaggatgaat cttgtgagaa gaagttctcc tttgtttgca agttcaaaaa 600
ctagaggaag ctgaaaaatg gatgtctaga actggtcctg caattactat gaagtcaaaa 660
attaaactag actatgtctc caactcagtt cagaccatct cctccctaata gagtttgcat 720
cgctgatctt cagtaccttc acctgtctca gtctctagag ccctgaaaaa taaaaacaaa 780
cttatTTTTa aaaaaaaaaa aaaaaggggg gcgctctaaa gatccaagct tacttcgcgt 840
gcatg                                         845

```

<210> 295

<211> 1046

<212> DNA

<213> Homo sapiens

<400> 295

```

ctgcaggccc cgggtccgga ttcccgggga agaagaggaa gaagaagagg acagccaggc 60
tgaagtcttg aaggatcatca ggcagtctgc tgggcaaaaag acaacctgtg gccagggtct 120
ggaagggccc tgggagcgcc caccctctct ggatgagtc gagagagatg gaggtctctga 180
ggaccaagtg gaagaccag cactaagtga gcctggggag gaacctcagc gcccttcccc 240
ctctgagcct ggcacatagg caccagcct gcctctccca ggaggaagtg gaggggacat 300
cgctgttccc cagaaaccca ctctatcttc accctgtttt gtgctcttcc cctcgcctgc 360
tagggctgcg gcttctgact tctagaagac taaggctggg ctgtgtttgc ttgtttgccc 420
acctttggct gataccaga gaacctgggc acttgctgcc tgatgccac ccctgccagt 480
cattcctcca ttcaccagc gggagggtgg atgtgagaca gccacattg gaaaatccag 540
aaaaccggga acagggattt gcccttcaca attctactcc ccagatctc tcccctggac 600
acaggagacc cacaggcag gaccctaaga tctggggaaa ggaggtcctg agaacctga 660
ggtaccctta gatccttttc taccacttt cctatggagg attccaagtc accacttctc 720
tcaccggctt ctaccagggt ccaggactaa ggcgtttttc tccatagcct caacattttg 780
ggaatcttcc cttaatcacc cttgctcttc ctgggtgcct ggaagatgga ctggcagaga 840
cctctttgtt gcgttttgtg ctttgatgcc aggaatgccg cctagtttat gtycccgggt 900
gggcacacag cggggggcgc caggttttcc ttgtcccca gctgctctgc cccttcccc 960
ttcttccctg actccaggcc tgaaccttc ccgtgctgta ataatcttt gtaaataaaa 1020
aaaaaaaaa aaaaaaaaaa aaaaaa                                         1046

```

<210> 296

<211> 1916

<212> DNA

<213> Homo sapiens

<400> 296

```

cggacgcgtg ggcgaacaga cgggtgcccta tggactgtcc aactacagag gaagcttccg 60
gggcaagagg tctgcggggc cacttccagg gaatctgcag ctctcacatc ggccacactt 120
gcgctgcgct tgtgtgggga gatatgacaa ggcctgcctg cacttttgca cccaaactct 180
ggacgtcagc agtaattcaa ggacggcaga aaaaacagac aaagaagagg aaggggaagt 240
tgaagtcaag gaccaacaaa gcaagcaggc ttttagacctc caccatccaa agctcatgcc 300
cggcagtgga ctgcacctc ctccatctac ctgccccgc tgcctcttcc aggaaggagc 360
cccttaggag gacaggcctg cagcatcctg gtctcgggag gcttctgtca ttgctcacac 420
acagttcaga tttccacctc tttatagaca agaagtgaat ttgcctgggg cagaacaccc 480
acccaaagag tcccactta acaatacccc cccacacggc aagaatgcc aaatccgaat 540
gacccaggtt ttctaataga gtaaatgat ccagatgtg cccagagca tgacgcctgc 600
agytccggtt tcatgcagga aattggtttt ggagagtttt ggcaagtgg aaagccactt 660
actggttttt gacatgactt ctcttgagga ataagtggac tccaagctaa ctctttgcaa 720
atgtaaacac atgtccatct tgtaataaat gcaaatgcc cgtgcagcag aagcatgcga 780

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ctttcatatc cttgcctaga ataggctgca tgggtgatgt cagtgagggc caccgagcgt 840
cggcttttaga cacagatcat agctctwyag gagtttatga atttgaagct tatgggattt 900
tggcagagaa attttcagct gtgcttgata cccaccaaaa gaatgtatct cgaaagaatg 960
aaggaagaag aaaaaaggat ccttgatggt tgtgacaaga aaatgagaaa gttagtatct 1020
gcaatacaga gcttggtcct gttcagtgac tgaccctctg tattctgtat agacaccagg 1080
ccgatacaca gtggagttcc caggccttgt ttgcaggaag ccgactgtaa agacagcccc 1140
agctcaaggc tattaggttg aatatttgct ttcagtagta aatgtggatc tttggggaat 1200
ggcttcaaaa taagtcacga acacaaattc tttgtaaatt atgtaaattc ctgtttatat 1260
aaattggcaa caacttatac cgtctgacag ttcaaaatct ctttcagctg cgctcttccc 1320
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aggggagggc tgcccctctc cccaacccag tcacagagag ataggaacg gcatttgagt 1440
gggtgtccag ggccccgtag agagacattt aagatgggtg atgacagagc attggccttg 1500
accaaatgtt aaatcctctg tgtgtatttc ataagttatt acaggtataa aagtgtgac 1560
ctatcatgag gaaatgaaag tggctgattt gctggtagga tttgtacag tttagagaag 1620
cgattattta ttgtgaaact gttctccact ccaactcctt tatgtggatc tgttcaaagt 1680
agtcactgta tatacgtata gagaggtaga taggtaggta gatttttaaat tgcattctga 1740
atacaaactc atactcctta gagcttgaat tacattttta aaatgcataat gtgctgtttg 1800
gcaccgtggc aagatggtat cagagagaaa cccatcaatt gctcaaatac tcagaaagta 1860
ctgtcaaaaag cctaataaaa aacctaaggt ttgctctgaa aaaaaaaaaa aaaaaa 1916

<210> 297

<211> 1476

<212> DNA

<213> Homo sapiens

<400> 297

gggattctcc tgtcttagcc tcctgagtag ctgtgattac aggcattgcgc caccatgcct 60
ggctaatttc atatttttta gtagagacag gatttctcca tgttggtcag gctgggtcttg 120
aactcctgac ctcagggtgat ctgcccact ckgcctmcta aaktgctggg attacaggca 180
tgagccactg cacctggccg gttattctst stttacagat agctatagac atcattttag 240
gaagtgttgc agtctggcat ttgtgctatt gttcattctc tgtgaaggct gttcatagtt 300
gctatagcct gtgtttagtt ttgtgatttc atcaatccca tctttctgtg tgagtaatgc 360
attctaaaca tcctacccca ctttagaaac ggacgtgggg aacgcttggg catttaagcc 420
aacaataaat ttaggtgaat gtccctaagt gtttastgtt tttatccagt caaggatttg 480
cttttccctg aacatttggt ttaaattctg gggccaaaat gcaaaggaga agttctattc 540
aaaggcagta gttgaaatct attatttttag ttagcctact tggcatttac tacatcggtc 600
acttctccag gctgccctaa attaggttga tggagtgaga catgccaaac atccaccttt 660
gggaccatag catagttaaa attaaatgta gttggaatag ctagcattgc agctacagta 720
gggaactgta gtctagttcc ctacagaaaa cccaaggrrg gaaggagacag gattttgcct 780
aggcaaaaat ctaagactcg tgccctcctg gtacatgggg ttttaagact gaatgtgtaa 840
taggagcact gcctttgcca aatcaaatga gtgacagggt aactagaaaa tgtgacaatc 900
acatttcctc ttagctcaaa taattctgtt tttccaaagc tttagcagct taattaaatc 960
tgttggactg ggggaggaga gagctgttct ctagtgggtt acatgggtatt ctttaagaag 1020
aaaaaaciaa gccaaagaaa actcattatc tggcatgttc gccttaagaa tgggtastggg 1080
tagaatctgg agttttcatc tcttttcaaa gctgcatac tctyatattt ggtattggcc 1140
tctaagtcta atattgcagt tggaattctt gctgtattat tttttaagca agtggttaggt 1200
gcatttaact gctttcttca tccatgacga cattcccacc atgggggtct tgacaaagca 1260
gagtaaaaaa atgctgttta cattgtttac ttacaagtaa ggagcctgaa ataacctgta 1320
gtttcgaatg caggccctga tttactggcg ttgtcagttt caattatgaa actgaagttt 1380
ggtgcctcct ctttatcatg tttttccct ttagcaggtt gtgtttaatg tcattaaaaa 1440
gaaataaaag ttctttgtca gtgaaaaaaa aaaaaa 1476

<210> 298
 <211> 541
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (175)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (178)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (249)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (506)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (524)
 <223> n equals a,t,g, or c

<400> 298
 tgcaggtacc ggtccggaat tcccgggtcg acccacgcgt ccgatttcaa aagctaatac 60
 tataatacat ttccataaaa atgatgtttt aagggtaaaa gaaaagaagt aagctatttt 120
 cctagataaa gctgccagct ctaacaagac ataaaacatg tttttcggcc taggnntntt 180
 atcaatttag agtggtaatg ctgggtcaga tgttttgatt aattaatctt tgattaataa 240
 gtataagana gctaattatt agaagagaag gttgttttat aaacatcatc tttcaaaatt 300
 cgagatttat ggggaataaa ttaggagaag gtggttaaac ctcttcaaca ataaattgct 360
 ctttggggac attttatgca cagaactgtg caccctctc agaacagcag gtctttaatg 420
 gcccatgtga tgagaagggc cccatcaagg cagcaggaat gggccactct cccacacccc 480
 atggggccagg ccaactgccac tcctgntgcc ctgcatcccc aggnnttatag gctgcatggt 540
 a 541

<210> 299
 <211> 471
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc feature
 <222> (437)

<223> n equals a,t,g, or c

<400> 299

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ctgccccatc cactagacaa aagctgactc tggaaaacat taggcactca gaatcaaggg 60
ttctggggtc agatggataa ttgccatcat cctcaccaag ttgccactgg actttcttgc 120
ccctaaatcc actgggcatt tcattgctac ctttcttgac ttcttgattg tttttgtgat 180
actgacacat cccccctttc agaacaccct ctgcccttgg attctgtgca caggaaagcta 240
gttgctcccc tgaatacact ctttcttcct tgtaatacag cctctgattt tgagcccaag 300
aataaaagact acagttctca gactccttcg caaataaatt ttgtgactaa actctagtca 360
acagtaagtg tcatgtagca gctcctggga atctccttta aaaagagagc ttgtttatac 420
cttattgtca tctctgntct tctgtgcccc ttcttcatt ttggctgcct g 471
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<210> 300

<211> 942

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (507)

<223> n equals a,t,g, or c

<400> 300

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ccatccttgt ctatttggc aagggctatt tctgtgcata ggcataggct tcagcagaat 120
tgacaggtact ggcagtcgga aattggacca gcaaacagaa atgattccta caggggatac 180
aagccaggca caggcagtg ctgttacttg gggttcctgt tgcttagagt tgaaagcatc 240
ataacccatc ccagggtgatc atagaaggac ctcaaaggaa aaggtgaggg gtttggacat 300
ttcctgagaa tccatggggg aaccattcag ggtttggggc aggtgtcaac cacaagaaca 360
ttaaacaggc tcttttgga gcaaagttgg gagtgtgtt gaagtaactg ggaaaactcc 420
acagaggctc agcgtccacc tctacctgac accctgccag caacctgggt gatttccgca 480
acagaggctc cccgatctc tcagtntat ggcccactg tgaoccaga aatgccacac 540
gggtgtctgaa cccgatctc tcagtntat ggcccactg tgaoccaga aatgccacac 540
catggaagcc acacactctg ctgtctcctt ctgtcctcat tcctgtcctt ctcamagtca 600
gtccctcttg gctcttccca gagtcccttt cattccctca ttcccaactt cctgccgctg 660
tactgtcacc tgtggccctg gatttgcact cttggtccaa caccctcaac tccaacacct 720
ctgtctttct gcccaccca ctagacaaaa gctgactctg gaaaacatta ggcactcaga 780
atcaagggtt ctggggctag atggataatt gccatcatcc tcaccaagtt gccactggac 840
tttcttgccc ctaaattccac tgggctttgt ttgcaacttt ctgataattt ataattattt 900
caaaataaaa aaattttaaa aataaaaaaa aaaaaaaaaa at 942
```

<210> 301

<211> 461

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1)

<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (345)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (363)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (444)
<223> n equals a,t,g, or c

<400> 301
nscakmcgag gstagctgag ggacgcagct agaccttggc gggacggggc tttcgccggg 60
gccagggccc agggaccagg cggaggcgtc gcgggagcct ttggggcacc acagagatgc 120
gggtttgcct gcaatgagat ttcattctct acatttaaag gacatccttt ctgagctgct 180
gtgaataaat ttggaatggt actgtatatt ttcataat ggagaactag ctgtactttg 240
aataaggatt gctgcactgg acgactttag aacatccctc acaatgtcgt caaccgggag 300
ccagaacccc cacggcctga agcagattgg cctggaccag atctngggac gacctcagag 360
ccnggcaccc agcagggtgt acacamgggc agagcatggg ccaagttcca gatatatgga 420
gytctaacag taatcctcct ggcntagcgc aggttgattg c 461

<210> 302
<211> 906
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (584)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (627)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (863)
<223> n equals a,t,g, or c

<400> 302
gctgactccc tctggtttcc ggtcaggctg gtcgggtcccc actatgggcc tggagctgta 60
cctggacctg ctgtcccagc cctgcccgcg tgtttacatc tttgccaaga agaacgacat 120
tcccttcgag ctgcgcacgt tggatctgat taaaggctcag cacttaagcg atgcctttgc 180
ccaggtgaac cccctcaaga aggtgccagc cttgaaggac ggggacttca ccttgacgga 240
gagtgtaggc atcctgtctc acctgacgcg caaatataag gtccctgact actggtaccc 300
tcaggacctg caggcccgtg cccgtgtgga tgagtacctg gcatggcagc acacgactct 360

gcggagaagc tgcctccggg ctttgtggca taaggtgatg ttccctgttt tccctgggtga 420
gccagtatct ccccagacac tggcagccac cctggcagag ttggatgtga ccctgcagtt 480
gctcgaggac aagttcctcc agaacaaggc cttccttact ggtcctcaca tctccttagc 540
tgacctcgta gccatcamgg agctgatgca tcccgtgggt gctnggctgc caagtcttcg 600
aaggccgacc caagctggcc acatggnngc aggcgtggag gcagcagtgg gggaggacct 660
cttccaggag gccatgagg tcattctgaa ggccaaggac gacttcccac ctgcagaccc 720
caccataaag cagaagctga tgccctgggt gctggccatg atccgggtgag ctgggaaacc 780
tcacccttgc accgtcctca agcaagtcca caaaagcatt ttcatttcta atgggccatg 840
ggagccaggc ccagaaaagc acngaattgg cttgcttaag acttgcccaa gttcccagag 900
cacctt 906

<210> 303

<211> 620

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (125)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (620)

<223> n equals a,t,g, or c

<400> 303

tggatgagta cctggcatgg cagcacacga ctctgaggag aagctgcctc cgggccttgt 60
ggcatcccgt ggggtgctggc tgccaagtyt tcgaaggccg acccaagctg gccacatggc 120
ggcancgcgt ggaggcagca gtgggggagg acctcttcca ggaggcccat gaggtcattc 180
tgaaggccaa ggacttccca cctgcagacc ccaccataaa gcagaagctg atgccctggg 240
tgctggccat gatccggtga gctgggaaac ctcacccttg caccgtcctc agcagtccac 300
aaagcatttt catttcta at gggccatggg agccaggccc agaaagcagg aatggcttgc 360
ttaagacttg cccaagtccc agagcacctc acctcccgaa gccaccatcc ccaccctgtc 420
ttccacagcc gcctgaaagc cacaatgaga atgatgcaca ctgaggcctt gtgtccttta 480
atcactgcat ttcattttga ttttgataa taaacctggg ctcagcctga gcctctgctt 540
ctaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600
aaaaaaaaaa aaaaaaaaaa 620

<210> 304

<211> 533

<212> DNA

<213> Homo sapiens

<400> 304

ggcacgagsg gcgggaacac gcggggccca agatggcggc cagccggtac cggcgttttc 60
ttaagctctg tgaggaatgg ccagtggacg agaccaaacg gggccgggac ttgggcgctt 120
acctgcgaca gcgggtagca caggcctttc gggagggaga gaatacccag gttgcagagc 180
ctgaggcctg tgatcagatg tacgagagct tagcgcgact ccattcaaac tactacaaac 240
acaagtaccc tcgccccaga gacaccagct tcagtggcct gtcgttggaa gagtacaagc 300
tgatcctgtc cacagacacc ttggaagagc ttaaggaaat agataaaggc atgtggaaga 360

aactgcagga gaagtttgcc cccaagggtc ctgaggagga tcataaggcc tgagctcagg 420
ccttacctcg tgcacatacc taggtgtgga gtcttgtaga ttgccatcgt caataaaact 480
gccccagttt ccccttgaaa aaaaaaaaaa aaaaaraaaa gaaaaaagtc gac 533

<210> 305

<211> 1374

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1232)

<223> n equals a,t,g, or c

<400> 305

aaacaggaaa taaatacgaa tgaaactgag ctctaagcag catgtaacct ggcctgcac 60
caggaaatag aggacttcgg atccttctaa ccctaccacc caactggccc cagtacattc 120
attctctcag gaaaaaaaaa aaggtcccca cagcaaagaa aaggaatagg atcaagagat 180
acgtggctgc tggcagagca agcatgaatt cgatgacttc agcagttccg gtggccaatt 240
ctgtgttggt ggtggcacc cacaatggtt atcctgtgac cccaggaatt atgtctcacg 300
tgcccctgta tccaaacagc cagccgcaag tccacctagt tcctgggaac ccacctagtt 360
tggtgtcgaa tgtgaatggg cagcctgtgc agaaagctct gaaagaaggc aaaaccttgg 420
gggccatcca gatcatcatt ggcctggctc acatcggcct cggtccatc atggcgacgg 480
ttctcgtagg ggaataacctg tctatttcat tctacggagg ctttcccttc tggggagggt 540
tgtgtgttat catttcagga tctctctccg tggcagcaga aaatcagcca tattcttatt 600
gcctgctgtc tggcagtttg ggcttgaaca tcgtcagtgc aatctgctct gcagttggag 660
tcatactctt catcacagat ctaagtattc cccaccata tgcctacccc gactattatc 720
cttacgcctg ggggtgtgaac cctggaatgg cgatttcttg cgtgctgctg gtcttctgcc 780
tcctggagtt tggcatcgca tgcgcactct cccactttgg ctgccagttg gtctgctgtc 840
aatcaagcaa tgtgagtgtc atctatccaa acatctatgc agcaaacca gtgatcacc 900
cagaaccggt gacctacca ccaagttatt ccagtgaat ccaagcaat aagtaaggct 960
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tctcaccttc attcttcaat tcagtctagg aaaccatgct gtttctctat caagaagaag 1140
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tatgtgggca tccagcctct ggggccttgg cnacacacat tcgtgtgctc tgctgcatgt 1260
gagcttgtgg gttagaggaa caaatatcta gacattcaat cttcactctt tcaattgtgc 1320
attcatttaa taaatagata ctgagcattc aaaaaaaaaa aaaaaaaac tcga 1374

<210> 306

<211> 668

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (558)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (575)

<223> n equals a,t,g, or c

<400> 306

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gcggacgtgg gcaggagggc tggaaaagcc ggcgctggag cgggaacggg agtagctgcc 60
tgggcgccaa aggccgcggc actcccacgc ggaccccgaa gtccgcaacc cggggatggg 120
cccgcggctg craggggatc ttctctggat caagcaatgg tggtgaaaaa tgtttcgcaa 180
gggcaaaaaa cgacacagta gtagcagttc ccaaagtagc gaaatcagta ctaagagcaa 240
gtctgtggat tctagccttg ggggtctttc acgatccagc actgtggcca gcctcgacac 300
agattccacc aaaagctcag gacaaagcaa caataattca gatacctgtg cagaatttcg 360
aataaaatat gttggtgcca ttgagaaact gaaactctcc gagggaaaag gccttgaagg 420
gccattagac ctgataaatt atatagacgt tgcccagcaa gatggaaagt tgccttttgt 480
tcctccggag gaagaattta ttatgggagt ttccaagtat ggcataaaag tattcaacat 540
cagrtcaata tgttaagtnat ataatttatt aaganaacta tgtttttagat aacagggaat 600
tcaggccatt aagagccccc ttataattag ggccactcct gtttgacagag tgattgggtt 660
gtaaacat 668
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<210> 307

<211> 1046

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (4)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (14)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (946)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (948)

<223> n equals a,t,g, or c

<400> 307

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cggnacgcgt gggncggacg cgtgggggttt tgaatgttca tgtatgaatg ctgcagctgt 60
gaagcataca taaataaatg aagtaagcca tactgattta atttattgga tgttattttc 120
cctaagacct gaaaatgaac atagtatgct agttattttt cagtgttagc cttttacttt 180
cctcacacaa tttggaatca tataatatag gtactttgtc cctgattaaa taatgtgacg 240
gatagaatgc atcaagtgtt tattatgaaa agagtggaaa agtatatagc ttttagcaaa 300
agggtgttgc ccattctaag aaatgagcga atatatagaa atagtgtggg catttcttcc 360
tgtttaggtg agtgtatgtg ttgacatttc tccccactct tccccactct gttttctccc 420
cattatttga ataaagtgc tgctgaagat gactttgaat ccttatccac ttaatttaat 480
```

```
gtttaaagaa aaacctgtaa tggaaagtra gactccttcc ctaatttcag tttagagcaa 540
cttgaagaag agtagacaaa aaataaaatg cacatagaaa aagagaaaaa gggcacaaa 600
ggattggccc aatattgatt cttttttata aaacctcctt tggcttagaa ggaatgactc 660
tagctacaat aatacacagt atgtttaagc aggttcctt gggtgttgca ttaaagttaa 720
tccaccttta ggtatttttag agcacagaac aacactgtgt tgatctagta ggtttctatt 780
tttcctttct ctttacaatg cacataatac tttcctgtat ttatatcata acgtgtatag 840
tgtaaaatgt gaatgacttt ttttgtgaat gaaaatctaa aatccttgta actttttata 900
tctgcttttg tttcaccaaa gaaacctaaa atccttcttt tamwananaa aaaaaaaaaa 960
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1020
aaaaaaaaaa aagggcggcc gtttta 1046
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<210> 308

<211> 1686

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (7)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (29)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (39)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (117)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1522)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1551)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1627)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1673)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1686)
<223> n equals a,t,g, or c

<400> 308
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aatgaactct aaatacatat ctttctttca atgttcataat caacaaagct ccaattnaat 120
ggtccctgga aaaaaaaaaa tcgttccatg ttgttcccag gtcccgttca agaagttctt 180
cccagttcga gtcaagatct cgttccagtt ccagagaacg ttcgagatct cgtgggtcga 240
aatcaagatc cagctccagg tccacagggg ctcttcttcc ccacgaaaaa gatcttattc 300
aagttcatca tcttctcctg agaggaacag aaagagaagt cgttctagat cttcttcac 360
tggtgatcgc aaaaaaagac gaacaagatc acggtcaccg gaaagccagg tgattggtga 420
aaacactaaa caaccctgag cccagggcca accctacgga acaccactac tttaccaga 480
cgccacaggt catcatctgg atcatcccat tctggttccc gttcaagttc aaaaaagaaa 540
taatgtatta aaatttacat cttaaaaaaa tccagtacag tgcatgaagc atatttttaa 600
agaagttggt gtcttacttg gtcagaagtg ctaaatctgc tagtagaggt gcatgccttt 660
cattgctttt caaaacaata cagctgtgtt tatttgtgaa gttaaaagta aatagcattt 720
taagccataa tgtcccaaaa tagatgttct gtcattcatt atttacaacc atttgcttca 780
tttaaaacca tttcagctat aacaaagtac tttgcttcct aatttaaacc catTTTTgtc 840
atttccaaat acatcctgtc cattggctaa gacaggatta cctaggcttg cctgaacttt 900
gggcatggaa gaaagactgg aaactagtgt gaaacaacat acttatggaa aagaaagtca 960
gcctttttat gctgttaaca gatgtcagag tgattctcac caaaaaaagt taaactatgt 1020
tgtaagcagc caactgtaaa tgtctatttt gaaattccct atgctaaggg tgccttagaa 1080
tcattgtgtc tcttttatcc agctttactt ttttgcctca catttaatgc aaaagaatct 1140
tgtgatgtct acaaggagag aagtgggata tattttcctt tctgacacat aatttggggc 1200
aaaaaagaaa gtcttaagag tttatctttt ctctgctgat acggttgctt gataaagaca 1260
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aatgcttatt gctgcatgat gntaagcaaa agtcwttatt ttycctatcm nttgaaataa 1560
gttatggctt aaaagcyttt ggarttatct tcaaaattaa aatctggtca catgagcttt 1620
aatTTgnttt ctggttttaa aaataaaaag ggttctctta cagtatttcc agngcaatgc 1680
aaggan 1686

<210> 309
<211> 1426
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1350)
<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1391)

<223> n equals a,t,g, or c

<400> 309

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tcttcactct gatgagggct cagacttgat aacgcccgtg gtgccccatc cctataggag 60
ctggtgagat tgcagcctgc tgcctcccct ccatcagcca cagctattgg atttcccacc 120
cagaatcttt aggtaaatga gatcatgatt ctggaaggag gtggtgtaat gaatctcaac 180
cccggcaaca acctccttca ccagccgcca gcctggacag acagctactc cacgtgcaat 240
gtttccagtg ggttttttgg aggccagtgg catgaaattc atcctcagta ctggaccaag 300
taccagggtgt gggagtggct ccagcacctc ctggacacca accagctgga tgccaattgt 360
atccctttcc aagagttcga catcaacggc gagcaccttt gcagcatgag tttgcaggag 420
ttcacccggg cggcagggac ggcggggcag ctccctctaca gcaacttgca gcacttgaag 480
tggaacggcc agtgcagtag tgacctgttc cagtccacac acaatgtcat tgtcaagact 540
gaacaaactg agccttccat catgaacacc tggaaagacg agaactatct atatgacacc 600
aactatggta gcacagtaga tttgttggac agcaaaactt tctgccgggc tcagatctcc 660
atgacaacca ccagtcacct tcctgttgag tcacctgata tgaaaaagga gcaagacccc 720
cctgccaaagt gccacaccaa aaagcacaa ccgagaggga ctcaactatg ggaattcatc 780
cgcgacatcc tcttgaaccc agacaagaac ccaggattaa taaaatggga agaccgatct 840
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amcaacagca gcatgacctg tgaaaagctc agccgagcta tgagatatta ctacaaaaga 960
gaaattcttg agcgtgtgga tggacgaaga ctggtatata aatttgggaa gaatgcccg 1020
ggatggagag aaaatgaaaa ctgaagctgc caatactttg gacacaaacc aaaacacaca 1080
ccaaataatc agaaacaaa aactcctgga cgtaaattt tcaaagacta cttttctctg 1140
atatttatgt accatgaggg gaacaagaaa ctacttctaa cgggaagaag aaacactaca 1200
gtcgattaaa aaaattatct tgttacttcg aagtatgtcc tatatgggga aaaaacgtac 1260
acagttttct gtgaaatatg atgctgtatg tggttgtgat ttttttcac ctctattgtg 1320
aattcttttt cactgcaaga gtaaccaggn tttgtagcct tgtgcttctt gcctaagaga 1380
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<210> 310

<211> 1493

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (975)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1483)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1492)

<223> n equals a,t,g, or c

<400> 310

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gatctttagt tctaaagggc aacttgactg tgagtaggag ggccccaag aaaggragga 180
aagtcacacac ccagctaacc acacaacagg gcttcattat ggaaatattt taacaaaagt 240
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<210> 311

<211> 2342

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2322)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2327)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2338)

<223> n equals a,t,g, or c

<400> 311

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cagacaacag gggaccccg gcccggcgcc agagccgagc caagcgtgcc cgcgtgtgtc 180
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cctgcgtgct cgcgaggatg cgtgttcgcg ggtgtgtgct gcgttcacag gtgtttctgc 240
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tcacctgctc tgctgcaggg gacagcagag gaagaccatg tggacctgtc actgtcttgt 600
acccttgtgc ctgcctcagg ggagcaggct gaagggtccc cagggtggacc tggagactct 660
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ag 2342

<210> 312

<211> 854

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (850)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (854)

<223> n equals a,t,g, or c

<400> 312

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tctcctaaag cttttattta acagtcaaaa aggatcggtt ttttttgctt ttttaacctt 180
gaattttttt aatttacact ttttagtttt aattttcttg tatattttgc tagctatgag 240
cttttaataa aaattgaaag ttctggaaaa gtttgaaata atgacataaa aagaagcctt 300
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tggcttctcc gcccttgtaa ggtgttcagt agagctaaat aaatgtaata gccaaaccca 420
ctctgttggg agcaattggc agccctatct cagtttattt tttcttctgt tttcttcttt 480
tcttttttta aacagtaaac cttaacagat gcgttcagca gactggtttg cagtgaattt 540
tcatttcttt cttatcacc cccttggtgt aaaaagccca gcacttgaat tgttattact 600
ttaaattgtc tgtatttgta tctgttttta ttagccaatt agtgggattt tatgccagtt 660
gttaaaatga gcattgatgt acccattttt taaaaaagca aggcacagcc tttgccccaa 720
actgtcatcc taacgtttgt cattccagtt tgagttaatg tgctgagcat ttttttaaaa 780
gaagctttgt aataaaacat ttttaaaaat tgtaaaaaaa aaaaaaaaaa aaaaaaaaaa 840
aaaggggggn cccn 854
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<210> 313

<211> 1501

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1387)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1395)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1399)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1438)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1497)

<223> n equals a,t,g, or c

<400> 313

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atcaaataaa gtccccgtgg tgcagccatc ccatgcggtc catcctctca cccccctcat 120
cacttacagt gacgagcact tttctccagg atcacaccgc tcacacatcc catcagatgt 180
caactccaaa caaggcatgt ccagacatcc tccagctcct gatatcccta ctttttatcc 240
cttgctctccg ggtggtgttg gacagatcac cccacctctt ggctggcaag gtcagcctgt 300
atatcccatc acgggtggat tcaggcaacc ctacccatcc tcaactgtcag tcgacacttc 360
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ccctcatcca gctattgtaa cacctcaggc caaacaggaa catccccaca ctgacagtga 480
cctaattgac gtgaagcctc agcatgaaca gagaaaggag caggagccaa aaagacctca 540
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aacaagnggc aaaangganc gttttttttt gggtttttta aaacctggaa tttttttnaa 1440
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t 1501

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<210> 314

<211> 1193

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (999)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1069)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1190)

<223> n equals a,t,g, or c

<400> 314

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gaaactgcct taacttgaaa gatgctgatt ccacagagtt taggccaaat gcccagttc 120
ctctggtgat tgatatgccc gagcacaacc ctggcaattt gggagggaaca atgagactgg 180
gaataagaag aactgttttc aaaactgaaa attcaatatt aaggaaactt tatggtgatg 240

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ttccttttat agaagaaaga cacagacatc ggttcgaggt aaaccctaac ctgatcaaac 300
aatttgagca gaatgactta agttttgtag gtcaggatgt tgatggagac aggatggaaa 360
tcattgaact ggcaaatcat ccttattttg ttggtgtcca gtccatcct gagttttctt 420
ctaggccgat gaagccttcc cctccgtatc tggggctgtt acttgacgca actgggaacc 480
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tgactgggaa taatggggac tgccctgtgag gcctctgaaa taattgaagg caagatgaag 660
gaactatctg aagaaatcac tacactctta gagaatccct ctgttctcca gcaaaccatg 720
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```

<210> 315

<211> 798

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (547)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (718)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (771)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (783)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (793)

<223> n equals a,t,g, or c

<400> 315

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ccaggatgtg aatgcagctg agactgggtc ttgtccctcc ctcttgctcc tcggattgat 180

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aacttgtagt caactacatg cttttgtcag ggaaccctgg ctgctggcct tctgggtccc 240
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tgggcttcga tctggtaccc atagctggac caatcatgac atcccagatg gggtcacgtg 360
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gtaatgtgca catgtaaaag attcaaatag tatatatata aggtgtacag taaaaaagta 660
aacttccctt catcccaagc ctggcagcat tccctgatgc cgactttctg ggtgtgggct 720
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tanggttcga atncctga 798

<210> 316

<211> 1935

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (37)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (38)

<223> n equals a,t,g, or c

<400> 316

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agatattatc agttccaaaa gtagatgatg aaatcctagg gtttatttct gaagccactc 180
cactaggagg tattcaagca gcctccactg agtcttgcaa tcagcagttg gacttagcac 240
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gtgragctgc atttgatgaa gtgaagatgg ctgcccatac catgggaaat gccactgtag 480
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attgtatttt gtggaagtt aagtttagca atatagactc taaaagcaaa ttaaattttt 1560
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cttctgaaat gtacatgtat acatgtacct actgagtgt atgtgatttt taaaaatgta 1860
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aaaaaaaaaa aaaaaa                                     1935

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<210> 317

<211> 1738

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (22)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1723)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1732)

<223> n equals a,t,g, or c

<400> 317

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tggaggggct gttcttggtg gtggatgaaa ttgtagatgg aggggtgatc ctagagagtg 180
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tccaccctta ctacctgtgg gatcgcttgc tggtttgtct tctctgtgtc ctggagcaaa 1080
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gagtcaggag aaaaccacct tcataaactg ctctgtgcaa agaggaataa aacatttttt 1620
ccaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1680
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<210> 318

<211> 1340

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (29)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (67)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1340)

<223> n equals a,t,g, or c

<400> 318

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<210> 319

<211> 784

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (511)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (603)

<223> n equals a,t,g, or c

<220>

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<222> (643)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (754)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (763)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (778)

<223> n equals a,t,g, or c

<400> 319

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<210> 320

<211> 3527

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (94)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (96)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1926)

<223> n equals a,t,g, or c

<400> 320

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cattgagttt ataaactttt ggtttgtaga cttcatattt gatcttttct cttccaatca 900
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<210> 321

<211> 1449

<212> DNA

<213> Homo sapiens

<400> 321

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tcaaaagaacc tctgtattac tggcaacaga ctgaagatga ttgacagta accatacggc 240
ttccagaaga cagtactaag gaggacattc aaatacagtt ttgcctgat cacatcaaca 300
ttgtactgaa ggatcaccag tttttagaag gaaaactcta ttcattctatt gatcatgaaa 360
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aaggactgac ctggccagag ctagtaattg gagataaaca aggggaactt ataagagatt 480
cagcccagtg tgctgcaata gctgaacggt tgatgcattt gacctctgaa gaactgaatc 540
caaatccaga taaagaaaaa ccaccttgca atgctcaaga gttagaagaa tgtgatattt 600

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tctttgaaga gagctccagt ttatgcagat ttgatggcaa tacattaaaa actactcatg 660
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cctgcttctg tttgcgccat gatgttgatg ccctactctg gcaaccacac tccagcaaac 780
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<210> 322

<211> 777

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (36)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (752)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (771)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (775)

<223> n equals a,t,g, or c

<400> 322

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cacacgcgcg cacgcagcca gcgagcggcc ggagcggacg gcagacgggg cgggcggcgt 120
cagggctcgca gcgtctacag ctgctcgggg gcggtttctt ggcggagggt tggccggctc 180
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gagatggcga aaactcacca ccagaaagtc gagaagaaaa agaaggagaa aacagtggag 480
aagaaaggaa agaccaagaa aaagggaagag aaacctaattg ggaagatacc tgatcatgat 540

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ccagccccca atgtgactgt cctccttcga gaaccagtgc gggctcctgc tgtggctgtg 600
gctccaaccc cagtgcagcc cccattatc gttgctcctg tcgscacagt tccagccatg 660
ccccaggaga agctggccty ctyccccaag gacaaaaaga araaggaraa aaaagtgtgca 720
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<210> 323

<211> 1214

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1203)

<223> n equals a,t,g, or c

<400> 323

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gcccattctc cctggcaagc actacctgga tcagctcaac cacattcttg gcatcctggg 180
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gaagtggagc tggggggcgt ggagagcccg gcgccctgc cacctccctg acccgtctaa 1140
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aancccgggg gggg 1214

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<210> 324

<211> 1046

<212> DNA

<213> Homo sapiens

<400> 324

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gattctagta atcaagcagc agccagagaa tgggagatta ctacaaggga agacataaat 180
tcaaagcagg ttgtacagt gaaagcagac ctggagtctg aatcttttctg accaaacctt 240
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ccaagaacaa ttggctatcc atggactctt gtttatggta ctggaaaaca tggcacaagc 360
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1046

<210> 325

<211> 674

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (465)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (666)

<223> n equals a,t,g, or c

<400> 325

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gaaacttgct aaagactcgg cataaaaaaca gatctccaac taaagacatg gattcagaag 180
agaaggaaat tgtggttttg gtttgccaag aagagaagyt tgtctgtggg ctgactaaac 240
gcaccacctc tgctgatgtc atccaggctt tgcttgagga acatgaggct acgtttggag 300
agaaacgatt tcttctgggg aagcccagtg attactgcat catagagaag tggagaggct 360
ccgaaagggg tcttcctcca ctaactagaa tcctgaagct ttggaaagcg tggggagatg 420
agcagccma tatgcaattt gttttggtta aagcagatgc tttnttcca gttcctttgt 480
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caaacttaca tgaagacttt accaccagat aaacaaaaaa gattagtcca gggaaaactt 600
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674

<210> 326

<211> 357

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (342)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (354)
<223> n equals a,t,g, or c

<400> 326
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<210> 327
<211> 1579
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (969)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1413)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1574)
<223> n equals a,t,g, or c

<400> 327
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tccggccccc cagaaccgc gccatcccc ggagcctccc cagagctggc cgcgcaggat 180
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<210> 328

<211> 2272

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2222)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2263)

<223> n equals a,t,g, or c

<400> 328

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ttagacagtt taaaggacaa actcaagaag gcacaacatg aaagagaaca acttgaatgt 300
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<210> 329

<211> 1320

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1256)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1275)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1290)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1298)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1302)

<223> n equals a,t,g, or c

<400> 329

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cctagtcccc agacctcact gctatatgtc ttctccctgg caggcaggat gacgcaaac 180
acgggtgatt tgaatggagt tgctatggcc tctaggccat cccagccac ccacgtcaac 240
gtccacatcc accaggagtc agctttgaca caactgctga aagctggagg ttctctgaag 300

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aagtttcttt ttcaccctgg ggacactgtg ccttccacag ccaggattgg ttatgagcag 360
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ctcagcttgg ggccctggac tgtgctgmtg gcctcaggct gtgccttctg ggcgggggtct 480
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ccagaaaagc artttgccca raaaaaaaaa aaaaaggcgg gcgctctaaa aggatncctc 1260
gaagggggccc aagcnttaag cgttgcatgn gaagtcanaa gncttttccc taatagtga 1320

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<210> 330

<211> 1860

<212> DNA

<213> Homo sapiens

<400> 330

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gaattacaag actcatggca ctggcgtaaa gttgttgttt atctaatac tgatgaaata 180
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aaactgattc cagtaagaat tttcagta taaccaagta ctggaaagtt cttcagataa 540
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atattgtttg tattatgaag ttggagtgtg gtctactgaa attatactct taaataaata 1800
tgtatgtagt gtgtaaatatt ttctaataaa ttcttttgat aaacwaaaaa aaaaaaaaac 1860

<210> 331

<211> 1576

<212> DNA

<213> Homo sapiens

<400> 331

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tgccagatcc cgtgcagtcc tggggaccct gagaagcacc gagccatccc tgaccaggga 180
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gtgaatttgg tcaagggacc taactctctg agttccaggt tccttatctt tcaaattggg 600
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<210> 332

<211> 576

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (34)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (467)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (556)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (567)

<223> n equals a,t,g, or c

<400> 332

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ccagtccag aaaagcctac agaaaacctg gggaacacca cactgaccac tgagaccata 180
aaagccccag taaagtccac agaaaaccca gaaaaaacag cagcagtcac aaagactata 240
aaaccttcag tcaagggtcac aggagacaaa tctctcacta ctacctcttc tcatctaaat 300
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gatggctcac agaaaggtat ccacgctgga cagatgggag agaatgnatt cattccctgc 480
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<210> 333

<211> 1311

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (743)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (764)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1221)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1245)

<223> n equals a,t,g, or c

<220>

<221> misc feature
<222> (1254)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1273)
<223> n equals a,t,g, or c

<400> 333
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cccacctacc actgtccgag tgacacacaa gtgttttatt cttccaatg actctatcca 540
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<210> 334
<211> 1118
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (10)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1115)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1117)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1118)

<223> n equals a,t,g, or c

<400> 334

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<210> 335

<211> 2266

<212> DNA

<213> Homo sapiens

<400> 335

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<211> 1132

<212> DNA

<213> Homo sapiens

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<222> (214)

<223> n equals a,t,g, or c

<400> 336

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<210> 337

<211> 2229

<212> DNA

<213> Homo sapiens

<220>

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<222> (2208)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2216)

<223> n equals a,t,g, or c

<400> 337

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<210> 338

<211> 3728

<212> DNA

<213> Homo sapiens

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<221> misc feature

<222> (3707)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (3713)

<223> n equals a,t,g, or c

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<211> 2674

<212> DNA

<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2646)

<223> n equals a,t,g, or c

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<220>
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<223> n equals a,t,g, or c

<220>
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<223> n equals a,t,g, or c

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<211> 1457

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<222> (1457)

<223> n equals a,t,g, or c

<400> 340

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<210> 341
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<220>
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<210> 342

<211> 1929

<212> DNA

<213> Homo sapiens

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<220>

<221> misc feature

<222> (14)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1894)

<223> n equals a,t,g, or c

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<221> misc feature

<222> (1913)

<223> n equals a,t,g, or c

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<221> misc feature

<222> (1918)

<223> n equals a,t,g, or c

<400> 342

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<210> 343

<211> 1561

<212> DNA

<213> Homo sapiens

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<221> misc feature

<222> (1311)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1538)

<223> n equals a,t,g, or c

<400> 343

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<210> 344

<211> 2982

<212> DNA

<213> Homo sapiens

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<220>

<221> misc feature

<222> (795)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1329)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1995)

<223> n equals a,t,g, or c

<400> 344

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<210> 345
<211> 1654
<212> DNA
<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (14)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (26)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (41)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1538)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1546)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1584)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (1630)
<223> n equals a,t,g, or c

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gagcaacttt attttatggt taccatattt ttaaaaagat tttttgtcag ggtgacttaa 180
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<210> 346

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (252)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (493)

<223> n equals a,t,g, or c

<400> 346

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<210> 347
<211> 3176
<212> DNA
<213> Homo sapiens

<220>
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<222> (2546)
<223> n equals a,t,g, or c

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<210> 348

<211> 1127

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1017)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1047)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1057)

<223> n equals a,t,g, or c

<400> 348

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<210> 349

<211> 2135

<212> DNA

<213> Homo sapiens

<400> 349

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<210> 350

<211> 1578

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1577)

<223> n equals a,t,g, or c

<400> 350

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<210> 351

<211> 974

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (935)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (971)

<223> n equals a,t,g, or c

<400> 351

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<210> 352

<211> 2601

<212> DNA

<213> Homo sapiens

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<221> misc feature

<222> (2520)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2572)

<223> n equals a,t,g, or c

<400> 352

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<210> 353

<211> 921

<212> DNA

<213> Homo sapiens

<400> 353

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<210> 354
<211> 1311
<212> DNA
<213> Homo sapiens

<400> 354
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<210> 355
<211> 2253
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (430)
<223> n equals a,t,g, or c

<400> 355
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tgtggcggtan agctatgcag cttgaaatcc aagtagcact aaattttatt atttcgtatt 480
tgtacaataa gcttcccagg agacgtgtca acatttttg tgaagaactt gaaagacttc 540
ttaagaagaa atatgaagg cactggtatc ctgaaaagcc atacaaagga tcgggggtta 600
gatgtataca catagggggag aaagtggacc cagtgtattga acaagcatcc aaagagagt 660

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gtttggacat tgatgatgtt cgtggcaatc tgccacagga tcttagtggt tggatcgacc 720
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<210> 356

<211> 1235

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1102)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1109)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1154)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1169)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1171)

<223> n equals a,t,g, or c

<400> 356

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tgaaaacagg agaggagaaa tatctsatac aagtgaaggg atactggaga gagaaattac 240
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ctggtttcaa cagacacaaa tttatatgtt aaccagttt tcttgccgtt ctgtaagtgt 360
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tgtcagaata gaatagaatt ggggttcgat cttaacaggc cagaaatgcc tgggttttwt 540
tgggttgttt ttgtttttgt ttttttatca aatcctgcct gactgtctgc ttgttttgcc 600
taccatcgtg acatctccat ggctgtacca ccttgctcggg tagcttatca gactgatgtt 660
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ttcagggggg gatattaatg gaaaaaattg gtccc 1235

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<210> 357

<211> 1408

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1396)

<223> n equals a,t,g, or c

<400> 357

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gccccacggg ggaagaaaca gaaaaagaca agaatgagac tgagaatgac tctaaagatg 180
ctgagaaaaa cagagaagaa tttgaagacc agtcccttga aaaagacagt gacgacaaaa 240
caccagatga tgaccctgag caaggaaaaat ctgaggtagg tgatttcaaa tcggagaaagt 300
ccaacgggga gctaagtga tctcctggag ctggaaaagg agcatctggc tcaactcgaa 360
tcatcaccag attgcggaat ccagatagca aacttagtca gctgaagagc cagcagggtg 420
cagccgctgc acatgaagca aataaattat ttaaggaggg caaagaggta ctggtagtta 480
actctcaagg wgaaatttca cggttgagca ccraaaagra agtgrtcatt aaaggaarta 540
tcaacaatta tyttaaattg ggtcaagaag ggaagtatcg cgtctaccac aatcaatact 600

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ccaccaattc atttgctttg aataagcacc agcacagaga agaccatgat aagagaaggc 660
atcttgcaca taagtctgt ctgactccag caggagagtt caaatggaac gggtctgtcc 720
atgggtccaa agttcttacc atatctactc tgagactgac tatcacccaa ttagaaaaca 780
acatcccttc atcctttctt catcccaacy gggcatcaca tagggcaay tggatcaagg 840
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aatgtggagc tgaggaaagc taagaaggat gaccagatgc tgaagaggag aaatgtaagc 1140
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<210> 358

<211> 872

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (803)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (813)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (871)

<223> n equals a,t,g, or c

<400> 358

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gctctgtagg cagtgatcgt ggacgtattg tggacactga ggaagagaaa gaagaggagg 180
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cgacaacctt accctcagga gaagcaaac ctcggaagac actcaaagag aagaaggaaa 480
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cctctgttaa ggaggagtct tcatcatcca aacctggaaa gaaaatccca gcaggagctg 720
tttctgtatt tttaggagac acggatgtgt ttggtgctgc ctccgttcca tcaactgaag 780
agccacagaa gcctgagcag ccnactccaa ggnaaagccc ctatggtccc cctcccactg 840
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<210> 359
<211> 1744
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (1744)
<223> n equals a,t,g, or c

<400> 359
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gcccgggtgct ttggtggctt gtttttccct gtctttaata ggaatcaagt gtgatatcat 300
gaattgatgg ggggaagatt aagaaggctt tgtaagacta taagttagtt tgctgtgaag 360
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ctgttttttag aatcttgaag gaattgaaat tagttttctg gctgattccc ttcccttcc 480
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cccn 1744

<210> 360
<211> 673
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
<222> (653)

<223> n equals a,t,g, or c

<400> 360

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accggccatg tcggaggtga cccggagtct gctgcagcgc tggggccagt tttaggagag 240
gcgccgactt cgactcttgg ggccagctgg tggaggcgat agacrrgtat cagatattag 300
caagacatct acaaaaggag gcccaagctc aacacaataa ttctgaattc acagaagaac 360
aaaagaaaaa ctaaggcaaa attgcaacat gcttgggaat tgcgagtga gctttacagt 420
ccacacagtc tcaagaagaa tttaaactgg aggacctgaa gaagctagaa ccaatcctaa 480
agaatattct tacatataat aaagaattcc catttgatgt tcagcctgtc ccattaagaa 540
gattttggca cctggtgaag aagagaattt gggaatttgg aagaagatk gaaagagggg 600
tggtgtctgg agcagggctt cctgattctt ttctctgctt agagttcccc ggnactttta 660
tttaccacaag gtt                                     673
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<210> 361

<211> 1324

<212> DNA

<213> Homo sapiens

<400> 361

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cgagagactg cttgctgcgg cagagacgcc agrggtgcag ctccagcagc aatggcagtg 60
acggcggttg cggcgcgggc gtggcttggc gtgtggggcg tgaggaccat gcaagcccga 120
ggcttcggct cggatcagtc cgagaatgtc gaccggggcg cgggctccat ccgggaagcc 180
ggtggggcct tcgaaagag agagcaggct gaagaggaac gatatttccg gtgaggctca 240
ccgggtccca agtccagccc tggatctccc aatggccttc caatccttaa actgccaatc 300
gccccaccgg ttccctacctg gtgccttggg cgcccatcc cccaacagaa ctcccgggcc 360
ccaatccagt ataccctaac ccttgatgtc ccgaccgttg ccacgtatag ggcactccca 420
gttacctgca caacagtttc aggccccaa accgtttcca ccggcgggtc tccaaaacaa 480
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<210> 362

<211> 678

<212> DNA

<213> Homo sapiens

<220>
 <221> misc feature
 <222> (14)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (469)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (490)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (658)
 <223> n equals a,t,g, or c

<400> 362
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 ctttaaagga ttcttgacta gtcgtgcaca tcagaactgc caggccccca gtggttctga 360
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 attaacacat actggtca 678

<210> 363
 <211> 5236
 <212> DNA
 <213> Homo sapiens

<400> 363
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 ttttattctg gctccagtga aggacawaca gacagagcta ggagaaacat ttggagaagc 180
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<212> DNA

<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<222> (336)

<223> n equals a,t,g, or c

<400> 366

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<213> Homo sapiens

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 aggggctaata ttttaggttc aagttcctca tgcttatcac cttggcctgc gctgccatga 1560
 ctgtcatctt cttcatcgtt agtcaggtaa cggaaaggcca ttggaaatgg ggcggcrtca 1620
 cagtccaagt gaacagtgcc tttttcacag gcattctatg gatgtggaat ctgtatgtct 1680
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 acggacccac tgagatctac aagttgacct gcaaggaggc ccaggagtag gaggtgcag 1860
 cgcccggctg ggacggtctc tccatacccc agcccctcta actagagtgg ggagcatgcc 1920
 agaragagct caatgtacaa atgaatgcct catggctctt agctgtggtt tcttgacca 1980
 gcggcatgga catttgtcag tttgcctctt gacggtagct tttggaggaa gattcctgca 2040
 gccactaatg catttgttat gataacaaaa actctggtat gacacatttt ctgtgatcat 2100
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aggctggtgt catagtcttc tcaactcctaa tccatgacca ctgttttttt cctattttata 2340
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tgctaaacta cccaagtaag atttactgta ttaaattggc tcgggtctga aaagcttttt 2580
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tccttaggct ggcaagggat gctcatatgc gtgacaacaa aggtggggag aacatcacgt 2940
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<210> 369

<211> 2411

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (2406)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (2407)

<223> n equals a,t,g, or c

<400> 369

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accctgtctg gggcagggag ggcacaggcc tgcacatcga aggtgggggt ggaccaggct 180
gccccctgcc ccagcatcca agtcctccct tgggcgcccc tggccctgca gactctcagg 240
gctaagggtc tctgttgctt tttggttcca cttagaaga ggctccgctt gactaagagt 300
agcttgaagg aggcaccatg caggagctgc atctgctctg gtgggcgctt ctcctgggcc 360
tggtcargc ctgccctgag ccctgcgact gtggggaaaa gtatggcttc cagatcgccg 420
actgtgccta ccgcgacct gaatccgtgc cgctggctt ccggccaat gtgactacac 480
tgagcctgtc agccaaccgg ctgccaggct tgccggaggg tgccttcagg gaggtgcccc 540
tgctgcagtc gctgtggctg gcacacaatg agatccgcac ggtggccgcc ggagccctgg 600
cctctctgag ccatctcaag agcctggacc tcagccacaa tctcatctct gactttgcct 660
ggagcgacct gcacaacctc agtgccctcc aattgctcaa gatggacagc aacgagctga 720
ccttcatccc ccgcgacgcc ttccgcagcc tccgtgctct gcgctcgctg caactcaacc 780
acaaccgctt gcacacattg gccaggggca ccttcacccc gctcaccgct ctgtcccacc 840
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```

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cccgaactttg gcaagctgga ggaaggcacc tacagctgcc tggccaccaa tgagctgggc 1320
agtgttgaga gctcagtgga cgtggcactg gccacgcccg gtgaggggtg tgaggacaca 1380
ctggggcgca ggttccatgg caaagcggtt gagggaaaagg gctgctatac ggttgacaac 1440
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aaccctgagg ctgcagtcgc agaaggggtc cctgggcagc tgcccccagg cctgctcctg 1560
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gctggggcct agctgggagg tggctgaag cagacagga atgggagagg aggatgggaa 2040
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tatcctggaa cctgtcctcc ctttctcccc aactatgcat ctgttgtctg ctccctctgca 2280
aaggccagcc agcttgggag cagcagagaa ataaacagca tttctgatgc caaaaaaaaa 2340
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa tcgagggggg gcccgtacc aatcgcccta 2400
catganngta t 2411

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<210> 370

<211> 421

<212> DNA

<213> Homo sapiens

<400> 370

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caccagggca gcacagaaat cttgctggga tgaggagctg caaacatgtg tggtcgactt 120
tttggccttc tgctctttct actctcaggg atgggggatt acaactaaag aagttgtctt 180
ttggccgggc gtggtggctc acgcctgtaa tcccagcact ttgggaggcc gagggcggtt 240
ggatcacaa gtcaggagat caagaccatc ctggctaaca cgatgaaacc ccgtctctac 300
taaaaaattc aaaaacattg gccggcgagg tggcgggcac ctgtagtccc agctgctcgg 360
gaggcttgag gcagaagaat tgtgtgaacc cgggaggcgg agcttgcaat gagcccagat 420
c 421

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<210> 371

<211> 523

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (402)

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<220>

<221> misc feature

<222> (404)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (440)

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<220>

<221> misc feature

<222> (461)

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<220>

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<222> (470)

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<220>

<221> misc feature

<222> (481)

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<221> misc feature

<222> (516)

<223> n equals a,t,g, or c

<400> 371

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ggtattttctg gggtttttttg tttttgttt ttgtcttttt ttgagacgga gcttgctctg 180
ttgcccaggc tggagtgccg tggcacgac tcggctcact gcaagctccg cctcccgggt 240
tcacgccatt ctctgcctc agcctcccga gtagttggga atacaggcgc ccaccaccac 300
gcctgggcta atttttttgt attttttttag tagagacggg gatttctactg tgttagccag 360
gatggtctcg atctcctgac ctctgatcc acccacctcc gntnccaaag tgctggggat 420
tacaggcgtg accaccgggn ctgggcgaag attccttttag natcctgatn cctctctggc 480
nagattaatt atataagaat aggggcctta atggtncatt aat 523
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<210> 372

<211> 395

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (205)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (217)

<223> n equals a,t,g, or c

<400> 372

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gccacgcccg gcttatttcg tatttttagt agagacgggt ttccgcatgt tggtcaggct 60
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ccgggtgtga gccaccgcgc ctagccctct aaacttttaa ataatcgtga aatgtatgcg 180
cagctgaagc gaattcagct atttncttct accttngtg tggaatttaa aatactgaac 240
ttgtgagatg aacctggtgg gcaccagttc tcaaacttct tggtcacagg acgcttgcac 300
tctcttaaaa tgtactgagg acacctaaaa gcttttgctc actgttggtt actactgcta 360
tttactaaca tagaaattaa acatattaaa atatt                                     395
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<210> 373

<211> 468

<212> DNA

<213> Homo sapiens

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<220>

<221> misc feature

<222> (421)

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<222> (450)

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<220>

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<222> (464)

<223> n equals a,t,g, or c

<400> 373

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ccttggcctc cttaaagtga gggattacag gcattaccca ctgtgccag tcactataga 120
gattattaca ttacaataaa gaaaaaaact ttcaggactc tcatggagag ctgaagtgtt 180
catgaatatc aagcagaaca ggagttaact gaatagactc aaccaataga aaattaaagc 240
aatttttttt tttttttgct taaaagattg ctgatccttt ttgtttctca gagttaagaa 300
aacttttctt ttgagctatt ttcagctttt aacaattgag taaagtatat tcctgtgaac 360
aaaatttgaa gcatatttgn ttctctttac ccgatttctc cagatttttg aaactatttg 420
ngagtattct taacttaatg gcaatatann tatttgcata agtncaat                                     468
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<210> 374
<211> 499
<212> DNA
<213> Homo sapiens

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<220>
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<220>
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<222> (284)
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<222> (491)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (492)
<223> n equals a,t,g, or c

<400> 374
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gggctggctg tcacttgttt ttaagttgtt aaagtgtctc cggggaagct aaacttaaca 180
caggactggt agagacacca ccttcctgtg ggtggggctg cctcctacct ggagcagcac 240
tcatctccac ctgggcactc cgtgnaaagg ggaggagac tctntggctg ncagatgagg 300
gtggccctgt ccgtgtgtnc ccaggggtgg gtcaacanca tttnttcctn tgccagggt 360
tagatggatt tnatTTTTnc cggggggaag ggaaggngct ctggtttngg ggatttgtna 420
atctctgggn aanacnangt tttnaaaga attttttagg gttnngtggt gtgtaggaaan 480
tntnctntn nnaggtttc 499

<210> 375
<211> 493

<212> DNA
<213> Homo sapiens

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<220>
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<222> (65)
<223> n equals a,t,g, or c

<220>
<221> misc feature
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<220>
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<222> (162)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (210)
<223> n equals a,t,g, or c

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<222> (285)
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<220>

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<222> (366)

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<220>
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<400> 375
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 ggcaagactc catctcaaaa agaaaagaaa agaagactct gnacctgtac tcttgaatac 180
 aagtttctga taccactgca ctgtctgagn aatttccaaa actttaatga actaactgac 240
 agcttcatga aactgtccac caaggtcaag cagagaaaaat aattnatttc catggggact 300
 taaatggaac ttntgngggg ttattathtt ncataathtt tttatttgga aatttttggn 360
 tggtttcttn taaanggtct tggtttnccc ngattttcag ggaaactttt tttgnttttt 420
 aggnnttcca cagtttacgg caatttgggt tnaaatatac tttntggggg accaaaattg 480
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<210> 376
 <211> 364
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (30)
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<220>
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<222> (134)
<223> n equals a,t,g, or c

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<220>
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<222> (202)
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<223> n equals a,t,g, or c

<220>
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<223> n equals a,t,g, or c

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<223> n equals a,t,g, or c

<400> 376

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gtggagggttg cagngagttg agattgtgcc attgcactcc agcctgggca acagagcaag 180
actctgtctt angaaaaaaa annnnnnnnn nnangaaaag caacatantg gggtttctgt 240
caatctgtcc tcggctgccc ttctcatttg ntgatgggac cttgaaagca agcttgctag 300
gtgccctctg nggctccagc ctttaccgga agtgtggngc atgtttttaa cttnagggaa 360
nccg                                     364
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<210> 377

<211> 152

<212> DNA

<213> Homo sapiens

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<222> (4)

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<221> misc feature

<222> (12)

<223> n equals a,t,g, or c

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<222> (18)

<223> n equals a,t,g, or c

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<221> misc feature

<222> (43)

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<222> (83)

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<220>

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<222> (109)

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<222> (124)

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<222> (125)

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<222> (147)

<223> n equals a,t,g, or c

<400> 377

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atctgttact gatcatgtaa acntgctcac accgctgggtg aagcctgtna cagaacttta 120
cctnntgttt tcgagcctat gagtgcnctc tc                                     152
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<210> 378

<211> 647

<212> DNA

<213> Homo sapiens

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<220>

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<222> (22)

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<222> (490)

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<222> (633)

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<220>

<221> misc feature

<222> (647)

<223> n equals a,t,g, or c

<400> 378

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gggtcgaccc acgcgtccnn gcaaattaga tacaaagtaa gcagaagaaa agaaataaga 120
attagagcag gaatcaatga agttgaaaat aggaactcaa tagagacaat caacaaagtc 180
aaaagctgat tatttgaaaa gattaataaa atcaataaac ctctaaccag gctaactaag 240
caaaaagaga aagaacataa attgctaata tcagaaatga aagagtggac atcactacag 300
atccccatgga cattaggagg ataataaagg aatgctctga acaactgtat gctcacatat 360
ttgataacct agatgaaatg gagcaagtcc ttgaaagaca caatctgccaa aaactcacac 420
aagaagaaat agaccatctg aataggccta tatctatctt aaaatttgaa tcaataatta 480
ataacttttn caaacagaaa gcactaggcc cagatgtatt tgctgggtgaa ttctacaaa 540
catataagga agacattata ccaattatct ataattctct ttggaggata gaagcagaag 600
ggaatacttt ctggcttatt ttgggagggc agnattactc taatacn 647
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<210> 379

<211> 416

<212> DNA

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<220>

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<220>

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<222> (314)

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<220>

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<222> (359)

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<222> (360)

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<222> (362)

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<220>

<221> misc feature

<222> (368)

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<400> 379

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actcagctaa gagcatcgag ggggcgccga gaggcaaggg gcggggacgg gcggtggctc 120
gcctcgcggc ggaccgccc cccgctccca agatccaact acgagctttt taactgcagc 180
aactttaata tacgctaatt gagctggaat taccgcggct gctggcacca nacttgcctt 240
ccaatggatc ctcgttaaag gatttaaagt ggactcattc caattacagg gcctcgaaag 300
agtccctgtat tgtnattttt cgtcactacc tccccgggtc gggaatgggt aatttgcgnn 360
cntgctgnct tccttggtat tgggaaccgt ttctcaggtc cctctccgga atcgga 416
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<210> 380

<211> 310

<212> DNA

<213> Homo sapiens

<220>

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<220>

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<222> (157)

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<222> (180)

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<222> (201)

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<222> (269)

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<222> (296)

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<220>
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<220>
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<222> (301)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (310)
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<400> 380
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tcagcaccac acttccaact agctttcctg gggccagcat agcttcnaca cctcctcttg 120
acacaagcac aactttttacc ccttctactg acactgnctc aactcccaca attcctgtan 180
ccaccaccat atctgtatca ntgatcacag aaggaagcac acctgggaca accattttta 240
ttcccagcac tcctgtcacc agttctacng ctgatgactt tcctgcaaca actggngcng 300
natctaccn 310

<210> 381
<211> 247
<212> DNA
<213> Homo sapiens

<220>
<221> misc feature
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<220>
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<222> (225)
<223> n equals a,t,g, or c

<220>
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<222> (226)
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<222> (228)
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<220>
<221> misc feature

<222> (238)

<223> n equals a,t,g, or c

<400> 381

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ccagtaagcg ggcccggcct gcggaggtgg gcggcatgca gctccgcttt gcccggtctt 120
ccgagcacgc caccgcccc acccggggct ccgcgcgcgc cgcgggctac gacctgtaca 180
gtgcctatga ttacacaata ccacctatgg agaaanggcc ccccnngngg aacgcatnag 240
atagtgt                                     247
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<210> 382

<211> 197

<212> DNA

<213> Homo sapiens

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<220>

<221> misc feature

<222> (132)

<223> n equals a,t,g, or c

<400> 382

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cctagcctca agtgatcctc ctgtntcaac ctcccaagta ggattacaag catgcgccga 120
cgatgcccag antccagaac tttgtctatc actctcccca acaacctaga tgtgaaaaca 180
gaataaactt caccag                                     197
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<210> 383

<211> 418

<212> DNA

<213> Homo sapiens

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<220>

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<222> (372)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (382)

<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (392)
<223> n equals a,t,g, or c

<220>
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<222> (405)
<223> n equals a,t,g, or c

<400> 383
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gattccacca ttgctgcagc tgctccacag ccctttttcag gacccaaaca accgcagccg 120
ctgttcccag gatggtgatc cgtgtatata ttgcatcttc ctctggctct acagcgatta 180
agaagaaaca acaagatgtg cttggtttcc tagaagccaa caaaatagga tttgaagaaa 240
aagatattgc agccaatgaa gagaatcgga agtggatgag agaaaatgta cctggaaaat 300
agttcgacca gccacaggtt taccctctgc caccttcaga ttttncaatg gaaagccagt 360
atcgcggggg antatggatg cnttccttgg angcccagag gaaantaatg gcatggta 418

<210> 384
<211> 204
<212> DNA
<213> Homo sapiens

<220>
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<222> (123)
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<220>
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<222> (156)
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<400> 384
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agagaactac aaggagttca gtgagctgct ccccaatcga cagggcctna agaaagccga 120
ctnctccttc tgggtccaagt acatctcgtc tctgangaca tctgcagatg gagccaaggg 180
cggagcagtc agcagagagt gaag 204

<210> 385

<211> 436
<212> DNA
<213> Homo sapiens

<220>
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<222> (333)
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<220>
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<222> (351)
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<220>
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<220>
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<220>
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<222> (408)
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<220>
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<222> (422)
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<400> 385
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agggcatccc cttcgcagct cccaccaagg ccctggaaaa tcctcagcca catcctggct 120
ggcaaggggac cctgaaggcc aagaacttca agaagagatg cctgcaggcc accatcaccc 180
aggacagcac ctacggggat gaagactgcc tgtacctcaa catttggtg cccagggca 240
ggaagcaagt ctccggggac ctgcccgtta tgatctggat ctatggaggc gccttcctca 300
tggggtccgg ccatggggcc aacttcctca acnactacct gtatgacggc naggagatcg 360
ccacacgcgg aaacgtcatc gtggtcacct tcaactaccc gtgtnnngncc ccttgggttc 420
tnaactggg gacgcc 436

<210> 386
<211> 257
<212> DNA
<213> Homo sapiens

<220>
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<222> (216)
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<222> (222)
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<220>
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<222> (239)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (240)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (242)
<223> n equals a,t,g, or c

<400> 386
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gatcgccgcg ctggtcattg acaatggctc cggcatgtgc aaagctgggt ttgctgggga 120
acgacgctcc ccgagccgtg ttcccttcca tcgtcgggcg cccaagaca ccagggcgctc 180
atggtggggc atggggccaaa aaggactcct actttnggca anaaaagccc aaaacaagnn 240
tnggttctct taaccct 257

<210> 387
<211> 541
<212> DNA
<213> Homo sapiens

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<220>
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<223> n equals a,t,g, or c

<220>
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<220>
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<223> n equals a,t,g, or c

<220>
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<222> (513)
<223> n equals a,t,g, or c

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<222> (522)
<223> n equals a,t,g, or c

<220>
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<222> (534)
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cttggctgtc tcagagaatc acattttgga agatgtgaac aaatgtgtca ttgctctcca 120
agagaaggat gnggatggcc tggaccgcac agctgngca attcgaggcc gggcagcccg 180
ggtcattcac gtagtcacct cagagatgga caactatgag ccaggagtct acacagagaa 240
ggttctggaa gccactaagc tgctctccaa cacagtcag ccacgtagaa gccagccgng 300
gaagccctca gctcggaccc tgcccagccc atggatgaga angagtttat cgatgcttcc 360
cgcctggtat atgatggcat ccggggacat caggaaagca gtgctganga taagggancc 420
cctgaggagt tggatgactc tgactttgag acaggaggat ttgatgtcag aagcaggacg 480
agcgtccaga cagaaganga tcagctgana gcnggccaaa gntgcccggg cgancaaggc 540
t 541

<210> 388
 <211> 437
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (238)
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<220>
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 <222> (279)
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<220>
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 <222> (357)
 <223> n equals a,t,g, or c

<220>
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<220>
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 <222> (386)
 <223> n equals a,t,g, or c

<220>
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 <222> (418)
 <223> n equals a,t,g, or c

<220>
 <221> misc feature
 <222> (427)
 <223> n equals a,t,g, or c

<400> 388
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 tctgcacagg ctctgaggcc tcctatgagc tgacacagcc accctcggtg tcagtgtccc 120
 caggacagac ggccaggatc acctgctctg gagatgcatt gccaaagcaa tatgcttatt 180
 ggtaccagca gaggccaggc caggcccctg tgcaggtgat atataaagac agtgagangg 240
 cctcaaggat ccctgagcga atctctggct ccagctcang gacaacagtc acattgacca 300
 tccagtgggg tccaagcaaa aaacaaagct gaatattact gtcatccaca aacacantgg 360
 gtttccccat gttgtatccc gnggangaac aactgaacgt cctagttcag cccaaggnc 420
 ccctcngta ctctgtt 437

<210> 389

<211> 435
<212> DNA
<213> Homo sapiens

<220>
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<223> n equals a,t,g, or c

<220>
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<222> (13)
<223> n equals a,t,g, or c

<220>
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<222> (31)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (42)
<223> n equals a,t,g, or c

<220>
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<222> (62)
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<220>
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<222> (155)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (215)
<223> n equals a,t,g, or c

<220>
<221> misc feature
<222> (234)
<223> n equals a,t,g, or c

<220>
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<222> (246)
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<222> (395)

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<221> misc feature

<222> (417)

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<220>

<221> misc feature

<222> (420)

<223> n equals a,t,g, or c

<400> 389

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anggattccc aatcagcttc tggtagaggaa cggccccctg aagcagatgg caaaaagggc 120
aactccccca acagcgaacc gccactcct aaganggcct gggcagaaac ctctcggcct 180
ccagagacag agccgggacc tcctgcccc aagcntcccc tccccccacc tcancggggc 240
ccgcgnggga actggggccc ccctggggac taccagatc gtnggggtct tcctgcaagc 300
ccccagcacc ttgaagttga ggatgaggct tggcggcacg acgaaagcan tcgtcttttg 360
aatttccttg gcattggacg ggnccggcga aggcnagaag aaaaggcggc cgtttttagn 420
tcttcgaggg gccag                                     435
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<210> 390

<211> 349

<212> DNA

<213> Homo sapiens

<220>

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<220>

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<222> (3)

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<220>

<221> misc feature

<222> (22)

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<222> (234)

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<223> n equals a,t,g, or c

<220>
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<222> (323)
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<400> 390
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acatgggnga ctgggctgtg nccacacact ggggaacccta cactacggaa aanagnggct 120
acctggagat caccaagaan atgggcagca nctccatgaa gtggagcctg anaactaact 180
tcctgcgcta ctggaccctc ncctatctgg ctctgcccac agtgaaccga ccangangcc 240
accctgtgc cccccacagg ggaactccga ngctctccc gtgctcnccc angggtgagt 300
ccgaggattg ccccatgct ggncaccggt ggtccgggg gattcccca 349

<210> 391
<211> 603
<212> DNA
<213> Homo sapiens

<220>
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<223> n equals a,t,g, or c

<220>
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<222> (502)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (506)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (540)

<223> n equals a,t,g, or c

<400> 391

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agctaagccc agatgccttc atccagatgg ctttgcagct ggcctactac aggatctacg 120
gacaggcatg tgccacctat gaaagtgcct ccctgcgcat gtttcacctg ggccgcaccg 180
acaccatccg ctcggettcc atggactcac tcacctttgt caaggccatg gatgactcca 240
gcgtcacgga gcaccagaag gtggagctgc tgcggaaggc cgtgcaggcc caccgaggct 300
acaccgaccg ggccatccgc ggggaggcct ttgatcgaca cctgctgggc ctgaagctgc 360
aggccatcga ggacctggtg agcatgcccg acatcttcat ggacaccttc tacgccatcg 420
ncatgcactt cacctcttca cagccaggtc ctgcaagaca gatgtgcatg tcttcggggc 480
cgtggtcccc acggctacgg gnctgntata acccatggag gccacataac ttctccctgn 540
cggctacaca gctgcgcgga gacaacgccg ccgctgggca tactgagaag gctctggaat 600
ctc 603
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<210> 392

<211> 479

<212> DNA

<213> Homo sapiens

<220>

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<222> (368)

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<220>

<221> misc feature

<222> (385)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (394)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (467)

<223> n equals a,t,g, or c

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caataaccgct ggtaccagat gctgtaccag gctggcgtct ttgcctcccg ctcttctctc 120
cgctgctgtc gcatccggtt cacctgggcc ctggccctgc tgcagtgcct caacctggtg 180
ttcctgctgg cagacgtgtg gttcggcttt ctgccaagca tctacctcgt cttcctgac 240
attctgtatg aggggctcct gggaggcgca ctaacggtga acacctcca caacatcgcc 300
ctggagacca gtgatgagca ccgggagttt gcaatggggg gcaactgcat tttgaaaaat 360
ggggattncc tgtcggggtc tgggnttgct ctgnagattc cttggcagtc tctgaaatcg 420
ggtctcagag agtaattact tggaaaggaa gtaaaaccag gcaaccnaaa ccccatgag 479

<210> 393
<211> 407
<212> DNA
<213> Homo sapiens

<220>
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<222> (26)
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<222> (65)
<223> n equals a,t,g, or c

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<220>
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<220>

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ccacagaccc aggcgtggg gccgaaattc ccaccagcac cgncgacacc tccaactcct 180
ccaatncagc tccgcctcca ggggaagggtg cggatgactt ggagggggag ttcactgagg 240
aaacgatccg naaccttgac gngaactact acgacccta ctacgaccn accagctccc 300
cggtcggaga tcggnccggg aatgccggng aaccaggata ccatctatgn agggatttga 360

ngacctcggg gcgagaaagg ccaaaaanggg ggaccattga ttttgag

407

<210> 394

<211> 256

<212> DNA

<213> Homo sapiens

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agccaggcaa ccttgtnngt aacgaccaca tctacaagtt atcgtncaaca gcccatgnca 120
tttgtaataa tnttcttcat agtnatnacc ctcataatng gtggntttgg ncaactgact 180
agttccctaa taatgggtgc cccgatatgg ggtttgcccg catnaaaca ctaagcttc 240
tgactnttaa cctcct 256

<210> 395
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<212> DNA
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tgtccagagc cccggnccatc ttcagccact cctcggccta cagcgtgtgc gcaagccggc 180
gcaacgtgcc tgacgacgtn ctgaggctgg tgaaacanac agacagcctg gtgatggnga 240
acttctacaa caattacatt tcctgcacca acaaggccaa cctgtcccaa gtggccgacc 300
atctggatca catcaaggag gtggcangag ccagancctg ggnttttggg gnggactttg 360
atggtgggtcc aagggtccct gagngctgn aggacgctnc aagtatccag acctgatcgc 420
tgancgttta agangaactg gacggaggcg gaaggcaagg gcncactggc ttgacaacct 480
gntgaggtct tcgaggcttg ggaacaagtc aacaaactta cacaggcttc cgaggaggag 540

ccatccggtg gacactgggtg gttctgcagg accaatacgg tatcttgggg cttcagctca 600
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<211> 252

<212> DNA

<213> Homo sapiens

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cgcaggaagc ccacggtggt cactcgagtc tccgccttca tcgactggat tgaggagacc 180
atagcaagcc acttagaaac caaaggccca ccttggcaat tncatgaatcg atcccacatc 240
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<210> 397

<211> 543

<212> DNA

<213> Homo sapiens

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 agaaagagag gatctttatg caaaaattca ggctggtgaa ggagagactg ctgttcttaa 180
 ccagttacaa gaaaaaaacc atacactaca ggagcaagta actcaactaa cagagaagct 240
 ggaagaatca gtcagaaaagt tcataaaca gccagggag aatttgcag gaccaggtac 300
 aagagcagaa gggcacntct tagagctggc acaagaccgt gttccttttc ctagaaaact 360
 agtggttcat ggaattttaa ttagtccatt taatggaang ccaggagaa gggctctccc 420
 agcttggacc ttaccggtta aaggccaaac cggaantttt actttcagcc gaggccgcaa 480
 aactggttcc aagggcnggt cttcagatcc atttgggnca cngttccaan ggctttacca 540
 ggt 543

<210> 398
 <211> 284
 <212> DNA
 <213> Homo sapiens

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<222> (277)
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tccccaatag tgcttatggg ggccctgant ttccagtag cttcttttct cccaccggga 120
ctccccctna attnagcagc ctattcctnt cccaagcttc gtggaagctt tccccctgct 180
tccttgtaag gccagggaag tgtntgaatg cggagaacag nnactccact gtggcgangg 240
gacaggacag gccactacct atgataacgc ctgcggnctc tttt 284

<210> 399
<211> 427
<212> DNA
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gacaatgaca atgataagtt tgaaggcaac tgtgctgaac aggatggatc tggttggtgg 120
atgaacaagt gtcacgctgg ccatctcaat ggagtttatt accaagggtg cacttactca 180
aaagcatcta ctccaatgg ttatgataat ggcattattt gggccacttg gaaaaccgg 240
tggatttcca tgaagaaaac cactatggaa ggtaaatccc attcaacaga ctcaaatg 300
gaggaaggac agcaacacca cctgggggga gccaaacagg tcagaccaga gcacntgcg 360
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ctttttg 427

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cgctctagaa ctagtggatc ccccgggctg caggaattcg gcacgaggaa tccggaagaa 120
aagttcaatc tggaaacatc aatgctgcc aagactattgc agatatcatc cgaacatgtt 180
tgggacccaa gtccatgatg aagatgcttt tggacccaat gggaggcatt gtgatgacca 240
atgatggcaa tgccattctt cgagagattc aagtccagca tccagcggcc aagtccatga 300
tcgaaattag ccggaccag gatgaagagg ttggagatgg gaccacatca gtaattattc 360
ttgcagggga aatgctgtct gtagctgagc acttcctgga gcagcagatg caccacaacag 420
tggatgatcag tgcttaccgc aaggcattgg atgatatgat cagcacccta aagaaaataa 480
gtatcccagt cgacatcagt gacagtgata tgatgctgaa catcatcaac agctctatta 540
ctaccaaagg catcagtcgg 560

<210> 401
<211> 584
<212> DNA
<213> Homo sapiens

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<222> (582)
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agaacttgga ccttctcgt tctgtcctcc gtttagtctc ctcctcggcg ggagccctcg 120
cgacgcgccc ggcccgagc cccagcgca gatggccgcg tttgaaggat gacctctagg 180
aagaaagtgt tgctgaaggt tatcatcctg ggagattctg gagtcgggaa gacatcactc 240

atgaaccagt atgtgaataa gaaattcagc aatcagtaca aagccacaat aggagctgac 300
tttctgacca aggatgtgat ggtggatgac aggctagtca caatgcagat atggggacac 360
agcaggacag gaacggttcc agnctctcgg tgtggccttc tacagagggtg caaactgctg 420
cgttntggta tttgatgtga ctgccccnaa cacattcaaa accctanata gctggagaga 480
tgaagtttct catncaggcc agtccccgag atcctgaaaa ctttccatct ggtggggttg 540
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<210> 402

<211> 334

<212> DNA

<213> Homo sapiens

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<222> (332)

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tgctgatgat ttcttccaag gaaccaaggc ggccctggct gggggaacca ctatgaatca 120
ttgaccacgt tgttcctgag cctgggacaa gcctgctcgc tgcctttaac cagtggaggg 180

aatgggccga cagcaagtcc tgctgtgaac tactctctgc atgtggacat cagcgagtgg 240
nataagggca tccagggagg agatggaagc gcttgtnaaa ggatcacggg ngtaaattnc 300
ttccttggtg ttacatgggc tttttgaaaa gnat 334

<210> 403

<211> 378

<212> DNA

<213> Homo sapiens

<220>

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<400> 403

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tggtccatct cgggcagaag ctggcagtgg tgggcctggc ttcaccttca ccttccgcag 120
ccccgaggag gtcttccggg aattctttgg gattggagac ccttttgacag agctctttga 180
tgacctgggc cccttctcaa gagcttccag aacgggggtc ccgacactca agcccccttct 240
ttacttctct tcctccttcc ctgggcatcc gattctcctc ctcatcttct ccttcaatcc 300
tggtctggtg ctttccctct gtttctactc tacacctttg tccaaggaag cccatcccca 360
ccccaaatcn tgaaaaac 378

<210> 404

<211> 300

<212> DNA

<213> Homo sapiens

<220>

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<222> (232)

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<222> (242)

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<222> (275)

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<400> 404

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agcgaagctt ttttctcaga atgaagtgtt ccctaactag ccgaggaaga actatgaaca 120
taaagtctgc aacatggaag gtattgcact gcacaggcca cattcacgta tatgatacca 180
acagtaacca acctcagtgt gggataaaga aaccacctat gacctgcttg gngctgattt 240
gngaaccat tcctcacccn tcanatattg aaatnccttt acataccaag actttcctca 300
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<210> 405

<211> 502

<212> DNA

<213> Homo sapiens

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<222> (145)

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<222> (148)

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<222> (167)

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<222> (200)

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<222> (252)

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<222> (285)

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<220>
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<222> (424)
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gctctggctc ccagggtgccg aatgtgacat ccagatgacc cagtctcctt ccaccctgtc 120
tgcattctgtg ggagacagaa tcacnatnac ttgccggggc agtcagncta ttgaaaactg 180
gttggcctgg tatcagcagn agccagggaa accccctaaa ttactcctaa tctctgatgc 240
ctcctctttg gngagtggag tcccatcaag gtccagcggc atggntctgg gacggaattc 300
actctcacca tttccagcct gcagctgaag nttttgcaat tattactgcc aacagtttat 360
agttatcctt acattttggc cagggcccag tggggtttca aagaattgtg gntgcaccat 420
tgtnttaatt ttccgcctt tgntggggcn ttnaatnggg actgccctnt tgtgtgccnt 480
gganaatttt ntcccggggg cc 502
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<210> 406

<211> 289

<212> DNA

<213> Homo sapiens

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<222> (92)

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<222> (237)

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cagttccatt ccagatagc agcccagacc tncgcttcag ttctagcaga agaattacat 120
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aaagtgattg cagaaaagga taagcagata aaacagactg aagattcttt aacaagtgaa 180
cgtgatcggt taacaagtaa agaagaggaa cttaaggata tacagaatat gaatttntta 240
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<211> 434

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tgatcttttc aagaaagcag gatggactat cattactcct ccaacaccaa tcatcccaga 180
cgatcatcca ctctgggatg tcatccaaat ggctttccat gaatgtctta atgctagatg 240
aaaaacgtgt tatgggtgat gccaatgaaa nttccaattc aaaaanatgtt tgaaaaagct 300
nggtntccta ccattaaaag ttnacattcn ttatgnccat tcccctggga agaagnttcc 360
attggctgga cctgcgaatg ttcnnggncc aaagcacctt acaanccctc tttggantga 420
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gccgnttggg caagatcaca gggctctggat ccaacggggc cgtgcncnccn agataanccn 180
gaagangttc ggtgggancc atcnnacgcc gtgtgtgtng atgtgattca cacatattct 240
tcncccatat ntcnccccg ntgtttcaga atgacccaag nagtgngcca tctggatttc 300
nntccangtg gaagaaaaga cngcccgnat gtaaaaanat gttcttncca ccatnactga 360
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cttattttta cnccggccnc ttccccacc ntganggt 458

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<212> DNA
<213> Homo sapiens

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 ctgccgcggg cggacacgcc agaggaggan gccggggaat ggccgcggtg tggcagcaag 180
 tcttagcagt ggacgcgagt ttcggacgca gtatatccgc ggcgagcca gctgctgcgg 240
 gaanaatgcc aagggtgggc acccccagcg ctgcttcggg antacctgaa gcttcngggg 300
 cntnttggtg ggccannnct acggnccctc tccnaancaa ggagtgtcc gtgcctataa 360
 caacagcatc gtccggaagt anccgcactt actctnggan cggntggaag gacttnggaa 420
 gaatnatccc ccnggnccct ngggggggccc gtgggggcanc ctctttcct tttcaaaaaa 480
 aaangcncnc canccanggt ggnggggggn aanattnaaa ccggggggccg tcttnttaaa 540
 aaaaan 546

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acattcacta cacaggtcgc tacgtttctg caacaaactg caaaattgtc caatcctgat 120
ctccggggagg gacagatggc caatctctcc ccttccaaag caggccctgn tccccgggca 180
gcctnncgcc gaggggccc ncccccaacc cacangcagg gagg 224
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<210> 411

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<212> DNA

<213> Homo sapiens

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gtcattcaga aataccatac tgtgaatggc cacaactgtg aagttagaaa agccctgtca 120
aagcaagaga tggctagtgc ttcatccagc caaagangtc gaagtgggtc tggaaacttt 180
ggtgggtggc gtggaagtgg ttctcgtggg aatgacaact tcggtcgtgg aggaaacttc 240
agtggtcgtg gtggctttgg tggcagccgt ggtgggtggg gatatgggtg cagtggggat 300
ggctataatg gatttggtaa tgatggaagc aattttggga agtgggtgga gctacaatga 360
ttttggggaa ttacaacaat cagtcttcaa attttgggac catgaaggga agaaattttg 420
gaagcagaac tctggcccta tggcgggtgga agccaatact ttgcaaaacc ncgaaaccag 480
gtggctatgg cggtcngca catcagtagc tatgcantgg canaaaattt aattaaggaa 540
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<211> 342

<212> DNA

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cacttacgcg cctgatatgt ctaggatgct tggaggtgaa gaagcaaggc ccaacagctg 120
gccctggcag gtctccctgc agtacagctc caatggccag tgggtaccaca nctgcggagg 180
gtccctggat agccaacagc tgggtcctna cggctgccca ctgcatcagt tcctccggga 240
tctaccgcgt ggatgctggg ncagcatgaa cctcttacgt tggcagagtt ccggttcgtt 300
gggcctncaa tgtctttnaa gattgttggt gcaanaagga nt 342
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<212> DNA

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taatatatta ccttgagttg ttccaaaggt cttatgttta ttggctggaa tttccaata 180
gcaatgagga gtcaaggaag agtttcctac tcaccggcag catctggaat agcagaccaa 240
ctttcctcat gctggggagc aaatcangtg ttgcagctaa ggggccatgc aagaagagct 300
gcaatggcca ttcccttcac ctggctacct cctctactct acagggcacc gagcccaatg 360
gagaaggtgn gagtggagaa gcagngatgt gatgaattac tttgcatggg agagaaatcc 420
ctccaccatc tcaagccccg gccactgtgc gagcctgtcg agaagcacag catttcttna 480
ggtggaaaaga ttataactgt aatgtgaggg taccctatgt ctgcaagntc actgactagt 540
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<222> (442)
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gaccccttct tggaatacaa caactacggc tgctactgtg gcttgggggg ctcaagcacc 180
cccgtggatg aactggacaa gtgctgccag acacatgaca actgctatga ccaggccaag 240
aanctggaca gctgtnaatt tctgctggac aaccctgaca cccacaccta ttcatactcg 300
tgctctggct ccgcaatcac ctgttaccac caaaaacaaa natnttaagc ctcccntttt 360
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tcaggacgcg nctgtccctc tgccggggac ccagagccgc cgngccgct ctgcctcctg 120
cgtgttagcc tcctctgcgc gctccngcag gcggccgtgg gagccgctng nggcagggac 180
ggcgcgagggc tgctgctgct gnncccggcc cgc 213

<210> 416
<211> 319
<212> DNA
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<222> (238)
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 ggcattggacg ataccctgtt ccagttgaag ttcacggcgn aganactggt agaaagctgg 180
 ccaagaaggc ggtgtaagga ctccaaggcg ganaggacca aagtgaagaa ggnccctntg 240
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<210> 417
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 gctcatcccg gtggccgccg cgcaggagcc tcccggagct gcttgttctc agaacacaaa 180
 caaaacctgt gaagagtgcc tgaagaacgt ctctgtctt tgggtgcaaca ctaacaaggc 240
 ttgtctggac taccagttta caagcgtctt gccaccggct tccctttgta aattgagctc 300
 tgcacgctgg ggagtttgtg ggtgaacttt gaggcgctga tcatcaccat gtcngtagtc 360
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<210> 418
<211> 183
<212> DNA
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ataattttta attatattga cattatcatc ttttatttta ctctacaat gattatgtga 180
gggaatttca taacatggga ccaccaccac ctgggcaagg aatgccccct taccaggaa 240
tggaacaacc tccacaccat cttactatc agcaccatgc tccacctcct caagctcatc 300
ccccttactc nggacatcat ccagtaccac ntgaagcaag atncagagat aaacgaattt 360
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 gatggggaga cggttcgaggt gaaggggaca tgggagagac ctgggggtgc tgcaccgttg 180
 ggctatgact tctggtacca gcctcgacac aatgtcatga tcagcactga gtgggcagct 240
 cccaatntnt tacgagatgg cttcaacccc gctgatgtgg aggctggtga gaatcccccc 300
 atgtgncagc aggagccttn ggginctacat ncccttgntt ttntgggtcc aaatctttcc 360
 acccccacaa tttgntctnn nattgggccc agaattctaa agnggggntg gccntaggat 420
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atcaccaatg acagcgtgac ttcttccgca cgtccaagaa gatgtaccgg cacaggccag 180
tcctcatggt catcagccat gcagcccccc acggccctga ggattcagcc ccacaatatt 240
cacgcctctt cccaaacgca tctcagcaca tcacgccgag ctacaactac gcgccaacc 300
cggacaaaca ctggatcatg cgctacacgg ggcccatgaa gcccatccac atggaattca 360
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gccattgccca cgggtcatcgt catcagcctg gtgatgctga ggaaagangc agtatggcac 180
catcagccac gggatcgtgg aggtttgatc caatgctcac cccagaaaaa cgtccctgaa 240
caagatgcag aaccatgcta tganaacca ctaccaatac tggacagatc aattaggttg 300
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81

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tgctcctggg gcagcgggtg ttggtgctag agctgagctg tgaagggtgac gacgaggaca 240
ctgccttccc aactctgcac tatgagctgt gacaangcag ccaacctgtc anctagctca 300
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<211> 237

<212> DNA

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gaatccccac aggtaatggg tcagaatctg tttacgaaaa gacgtgacag taatcgaggg 180
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ccctgcntct naaaggnggg ggctcagatg gtgcggcctg agtntgcggc cggcggcatt 180
tgggatacac ccgtagggac ggggtgtntc ccaggcctaa ttccatcttt ccaccatgac 240
agaaatgccc ttttnaaggc tggcctcctt ggcgccctgtt cccacggcc cccgcagcgt 300
gagccacgat gcttccccan accccaccca ttcccgnaac acntacttac tgtnttggtg 360
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ncacaaacaa catcgaccca gtgggnaaga atccaaatga gacacaagga ggtcactgng 180
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ctgcagcatg aactgcaagc tcccctcagc ccatcttget ccctcttcag cccgctgagg 180
agctttcttg ggctgcccc atctctcca acaagggtga catattctgc gtagatgcta 240
gaccaaccag cttcccaggg ttcgtcgtg tgaggcgtaa gggacatgaa ttctagggtc 300
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ttctctaact tgnaaaaata ggtcacgggt ctagatcaca ttctcgatcc agaggaaggc 180
gatactctcg ctcacgcanc aggancangg ggacgaagggt caaagggtcan catcttcttc 240
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ctcctctggg ctcaaagcag ggaggcctct ctcttcctga atccgatgga aggggtgggag 120
gcctagggca ccttccggta ccttttccaa agatgccttc ntccgtccct gcatgacctg 180
gggtgagtc ttcctcgnnn tgtnc 205

<210> 433
<211> 424
<212> DNA
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<220>
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gaacgtgtaa gtttttatat atacagtttc caagccaact tcggggaagc cttaaccttt 180
ttacgggggtg ggggtgggga ggtaaaaagt tgtgatctct gagaaaataa ccgccactac 240
tctggaagtg ttcacagca gttatacaaa accgtgattt tggctgctcc ctaacaantc 300
gtgattgcat gattcgantg ncagtctgta gangaattgg gcttgggtgt acgtgtgttt 360
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gggg 424

<210> 434
<211> 415
<212> DNA
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ctcataaaaaa tggaaagcat ggcagcctca ggttggtaca gagtactcta ctccaaagta 180
aaagttattc tctgagaaag tgcttactgc cttttctgtt ctctagtttg cttgttttaa 240
catttactcc acaaaattgc tcaaacttac ccatctttga atatctagcc tctgggatga 300
gacagatgat ctttctccgt tttcactttt tatagaatac agctacctac ccangcaata 360
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<210> 435

<211> 612

<212> DNA

<213> Homo sapiens

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<222> (591)

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cctttgtctt tagtgagga cacacatatg cttacaccta cctttatcac cattcgttca 180
tgaatcatgc ctagctccat ccttgccctg ggacctacta ggccttcac caactgggaa 240
atggggagaa gcaaagctgg cctcatgctc ttcagggtca gttcctatct ggagttgacc 300
aggcctaccc cagttgccat tcctgaaaaa tctcagctgc caggctgcct ttaggggtccc 360
tgtagaccca ggagagttga gaggggtggg gacacagaga gaatagagag gatgtgggaa 420

ctggcagagg gccggagcgc angagttcaa gtggaggaat gctggctttg aaccctntac 480
actgctggnt gnatgacctt ggacaagcac ttcacctttt tgnggcttaa catcctcatc 540
tataaatggg gatctctgaa ccttctacct actacttaca ggctgtgtga ngaccaggag 600
tttgatttg ga 612

<210> 436

<211> 520

<212> DNA

<213> Homo sapiens

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<222> (156)

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atgggaaaca ttagggctgg gttcatgnaa aggggnccag cnttgnccg acngagggtta 180
anccntggga aggttatact ttggaggagg acctaagttg ctggctngcc tgatnttcaa 240
aacccttgcc cttgcgngna ccancnaga gactcttaat canggacaaa gncngctgn 300
ctantcaccg attttngatt ctnaaacaaa tgngtcacaa agtaagggat tctgangggg 360
ntatncaga caaaactgng ctagacatga ggggtctatgg ctaagagca ncagtgtgg 420
gcctggagca acaaattgct ttgatgtgca aaccctttaa caacagttta ttcagaagac 480
actttttccn agccaaaang tcttgatgc aanctgncna 520
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<210> 437

<211> 472

<212> DNA

<213> Homo sapiens

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tcccatgggg ccacctggtc cttcaggnc cagaggtcct caaggtccca atggagctga 180
tggaaccacaa ggacccccag ggtctgtttg gttcagttgg tgggtgttga gaaaaggggtg 240
aacctggagt aagcagggaa cccagggcct cctggggtaa gcaggtgtta ggcgggtccc 300
aaagtngnna agaggtngag aaaggnngaa ngntgntttc aacctngnc ttnttgggna 360
cctcncagtn gnccanggg nccaccaggt nttgttttgg ccctaagggn naaccgggt 420
nctttttngt ttttntngn nattctggnn ttttggggg attttgggnc ct 472

<210> 438
<211> 183
<212> DNA
<213> Homo sapiens

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<222> (178)
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ggttcaccag gtnccgntgg gttgccaggg tccatgggggt cccagggcac cccatctntt 120

gatcacgggt tnacttgngg accaggcata gttcaaacia tagatgaccn acattgtnc 180
ttt 183

<210> 439

<211> 541

<212> DNA

<213> Homo sapiens

<400> 439

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aagcataata tagcaaggac taaccctat accttctgca taatgaatta actagaaata 180
actttgcaag gagagccaaa gctaagaccc ccgaaaccag acgagctacc taagaacagc 240
taaaagagca caccctgcta tgtagcaaaa tagtggaag atttataggt agaggcgaca 300
aacctaccga gcctggtgat agctggttgt ccaagataga atcttagttc aactttaaat 360
ttgcccacag aacctcttaa atccccttgt aaatttaact gtagtccaa agaggaaacag 420
ctctttggac actagggaaa aaaccttgta gagagagtaa aaaatttaac acccatagta 480
gggcctaaaa gcagccacca attaagaagc gttcaagctt caacaccac tacctaaaaa 540
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<210> 440

<211> 301

<212> DNA

<213> Homo sapiens

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cctcaattgg ctggagggca gatctcgcga gtagggcaac gcggtaaaaa tattgcttcg 180
gtgggtgacg cggtagacgt gcccaagggc gttcgtaacg ggaatgccga ancgtagggaa 240
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t 301

<210> 441
<211> 365
<212> DNA
<213> Homo sapiens

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<220>
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<222> (357)
<223> n equals a,t,g, or c

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tatgcaaaac atcaaagtga attttccatg aatgttttta atattctcat ctcaacattg 120
tgatatatgc tactaaaaac cttttcatat acatcttacc tcatttcaag tgaattattt 180
taatcttkkt ctctctktcc aaaaawttag gaatgtttag tgtaattgga wttcgctatc 240
agttcccawc cttaagtttt gatattcaat atctgatagr wacaytgcat cyttggtcat 300
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aaaac 365

<210> 442
<211> 535
<212> DNA
<213> Homo sapiens

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ttcatgtctg tcttcctggc tcaggagaaa gaagaggctg ttgagggtcc gactccctac 180
ttggacttct ggacacagaag gggctgagtg actccttgag tagcagtggc tcttcctaga 240
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caagaagcca gaactgttgg gaatgaatcg cagccctcct tggagaggca gcctgtttat 360
tgattacaga ggtaagttta caaattgatt aggctataat taantgcaca tttccnccac 420
aggccnggca tgaaggccca gtgggttttc aaaggccaca ttncaccccc tntctgcctt 480
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<211> 387
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<400> 443

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ctgggggaac taagccggag gcagtggtag tggcggcggc gcaaggggtga gggcggtccc 120
aaaaccccgag gtaggtagag caagaagatg gtgtttctgc ccctcaaatg gtcccttgc 180
accatgtcat ttctactttc ctactgttg gctctcttaa ctgtgtccac tccttcattg 240
tgtcaganca ctgaagcatc tccaaaacnt antgatggga caccatttcc ttggaataaa 300
atacgacttc ctgaatacgt catcccagtg caatataaat ctcttgatcn atgcaaacct 360
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<211> 313

<212> DNA

<213> Homo sapiens

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<222> (275)

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<400> 444

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attaaatttg gatgtagtga natctctctc tgtaanaaaa cgcttatttt ctcccctaaa 120
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tggaatgatg aacgcttctt ctctcctctg ccatatgcc ctttgaaaag ttacatgtct 180
ctctattact tggcaataat ggggaattttt atttctacag ttgtattgtt ttggctctgct 240
ccataccctg taaacatttc cattgttcta caaannctgt gttctctttt ctgtcaaggg 300
tcangtgtn naa 313

<210> 445

<211> 72

<212> DNA

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<211> 406

<212> DNA

<213> Homo sapiens

<400> 446

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ttgtaatcat aaatactgct gtataaggta ataaaactct gcacctaata cccataactt 180
ccagtatcat tttccaatta attatcaagt ctgttttggg aaacactttg aggacattta 240
tgatgcagca gatgttgact aaaggcttgg ttggtagata ttcaggaaat gttcactgaa 300
taaataagta aatacattat tgaaaagcaa atctgtataa atgtgaaatt tttatttgta 360

ttagtaataa aacattagta gtttaaaca aaaaaaaaaa aaaaaa 406

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<212> DNA
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atggtcctcc atactcctca gacaacagcc ttncgaaagc aacctgtccc tacctgcaga 120
tgattancca tctatgaacc ggctgggtan gcaacaagtg ccatctttca tggagctgag 180

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<210> 448

<211> 536

<212> DNA

<213> Homo sapiens

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ggaaattgtg ggcataaagc ttaaaatccg tgggtttatc caaattgttg aaaccataa 180
gttaagttaa taaatgcctg ctttttgta ataataaatt ggtaaaagtt gcctaaccaa 240
aattaagttc ctccaagcca cctggaaaaa aagggttaatt ggantacccc tcctttaaaa 300
aaggnaaaagg cccaaccttt ttnggaaggt taagggtggn ttttngccta aaggcccctc 360
cagggaaaaa aatanncccg gtcccgggaa gaaanttttg ggttnaaaan cccgggtttt 420
nggaataaaa aggggaagng nttaacctt tccccgggn tttttccct tgggggtttt 480
ccaaaaaat tttttcccaa agggtttnc caaaaaaatt ttttaaagg tttttt 536

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<212> DNA
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aaggcccgna ngcctgganc ttgg 84

<210> 450
<211> 423
<212> DNA
<213> Homo sapiens

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atgggtgggcg cccctccac agcctcgtcg ccgccttgca gtttgatctc agactgctgt 180
gctagcaatc agcgagactc catgggcgta gggccctccg agccagggtgc aggatataat 240
ctcctggtgc accattcttt aagcccgtcg gaaaagcaca gtattagggt gggagtgacc 300
caattttcca ggtgccgtct gtcaccctt tctttgacta ggaaaggac ctccctgacc 360
ccttgcgctt cccgagtga gcaatgcctc aacctgcttc ggctcacgca cgggtgggctg 420
cac 423

<210> 451
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<212> DNA
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atatatatga aaataaaatg ttataattga cttcagtgtc ccataaaacca gcttcaacaa 180
ttaccaaatt gtgaccaatc tttacacaca tgcacagggg tccctcaata tctgtgggca 240
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cacttataat acgtaatacn atgtaaatgc catgtaaata ctgttatact gnattaangg 420
aataacaacc aggaaaaatg nacatgggtca agtaccagac cccaattttt ttgggggggg 480
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cntg 544

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gactcactgg gctgcacaga gctccgctag ctctgctgac agctgccact cattggcagg 180
gggtgggcct cttgtcttcc acacaagggt gaagtgggtcc tgggtgctcct tgtctgggg 240
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agcaccttca gtgccccgtg ggctgcctgg cccacagccg tgagcaagta ctgcctggct 360
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ttgaggaaaa ccacantgcc ntnagatcca 90

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gacccaact gctcttgccg cactggtggc tctgcaact gcgccggctc ctgcaagtgc 180
aaanagtgca aatgcacctc ctgcaagaag agctgctgtt cctgctgccc cgtgggctgt 240
gccaaagtgt ccaggggctg cgtctgcaaa ggggcacnag aaaaatgcag ctgctgtgcc 300
tgatgtggga acagctcttc tcccagatgt taatagaaca acctgcacna cctggatgtt 360
tttaaaaata cnacactgaa ccattgctgg catttccttt ttatactaaa tatgtgactg 420
aacaataaaa acattttgac ntttaaaaaa aaaaaannaa atttnnaaaa aaaaaaaaaa 480
cccggggccc ccaaaaaaca                                     500

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<210> 455

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<212> DNA

<213> Homo sapiens

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tattatcaag tgtcaagatc agcaagtgtc cttaagtcaa acagggtttt tttgttgntg 180
tttttgcttt gtttcctttt ttagaaagt ctagaaaata ggaaaacgaa aaatttcatt 240
gagatgagta gtgcatttaa ttatttttta aaaaactttt taagtacttg aattttatat 300
caggaaaaca aagttgttga gccttgcttc ttccgttttg ccctttgtct cgctccttat 360
tctttttttg gggggagggg tatttgcttt tntatcttcc tggcataatt tccattttat 420
tcttctgagt gtctatgnta acttcctct atcccgtta taaaaaatt ctccaacaaa 480
aatacttggt gacttgatgg tttatcactt ctctaannaa ggtgaaatac cctaattggaa 540
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ctgtggccac actgtgagga gatcggttct gggtcggagg ctacaggaag actcccactc 180
cctgaaatct ggagtgaaga acngccgccn tccagccacc attccaagga ggtgcatgag 240
aacanctctg tgataccatt taacttngtt gacattactt ttatttgaag gaacgtatat 300
tanancttac tttgcna 317
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taaaatggta gttagatctg gaggtctgat tttgtggcaa aaatacttcc taggtgggtgc 180
tggtgtacttc ttgtgtcatc ctgtcaggag gcagataatg ctggtgcctc tctattggta 240
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atgttaagac tgctgggtgg gtttggagtt ctgggnttta atcattcatt acaaagntca 300
acattttacc tgacgnntna ag 322

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<212> DNA
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cagtatctca agatattcag gnggccagaa gagcttgtca n 161

<210> 459
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<212> DNA
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<400> 459

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gcacccgaga ccgcagccgt ggccggagcc tggagcgggg cctggaccac gactttgggc 180
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agggcgggg cccgccacga tgcccgtctc tcggggaacc ccgaaagccg cagccgcgaa 360
gcacccgcat tcaaggagcc ccagncccga gcttaagggg cggcggggcc catcggttc 420
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485

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<210> 460

<211> 65

<212> PRT

<213> Homo sapiens

<400> 460

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Glu Gly Ser Tyr Thr Ser Ser Met Lys Gly Ser Leu Ser Val Thr Lys
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Leu Gln Ile His Lys Pro Phe Val Ser Pro Asn Leu Leu Gly Met Asn
 35 40 45

Pro Thr Tyr Ile Phe Ile Cys Val Gln Ala Thr Trp Phe Ser Leu Cys
 50 55 60

Tyr
 65

<210> 461
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 <212> PRT
 <213> Homo sapiens

<400> 461
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Val Ile Ser Ser Asp Ser Ser Pro Ala Val Glu Asn Glu His Pro Gln
 20 25 30

Glu Thr Pro Glu Ser Asn Asn Ser Val Tyr Thr Ser Phe Met Lys Ser
 35 40 45

His Arg Cys Tyr Asp Leu Ile Pro Thr Ser Ser Lys Leu Val Val Phe
 50 55 60

Asp Thr Ser Leu Gln Val Lys Lys Ala Phe Phe Ala Leu Val Thr Asn
 65 70 75 80

Gly Val Arg Ala Ala Pro Leu Trp Asp Ser Lys Lys Gln Ser Phe Val
 85 90 95

Gly Met Leu Thr Ile Thr Asp Phe Ile Asn Ile Leu His Arg Tyr Tyr
 100 105 110

Lys Ser Ala Leu Val Gln Ile Tyr Glu Leu Glu Glu His Lys Ile Glu
 115 120 125

Thr Trp Arg Glu Val Tyr Leu Gln Asp Ser Phe Lys Pro Leu Val Cys
 130 135 140

Ile Ser Pro Asn Ala Ser Leu Phe Asp Ala Val Ser Ser Leu Ile Arg
 145 150 155 160

405

Asn Lys Ile His Arg Leu Pro Val Ile Asp Pro Glu Ser Gly Asn Thr
 165 170 175

Leu Tyr Ile Leu Thr His Lys Arg Ile Leu Lys Phe Leu Lys Leu Phe
 180 185 190

Ile Thr Glu Phe Pro Lys Pro Glu Phe Met Ser Lys Ser Leu Glu Glu
 195 200 205

Leu Gln Ile Gly Thr Tyr Ala Asn Ile Ala Met Val Arg Thr Thr Thr
 210 215 220

Pro Val Tyr Val Ala Leu Gly Ile Phe Val Gln His Arg Val Ser Ala
 225 230 235 240

Leu Pro Val Val Asp Glu Lys Gly Arg Val Val Asp Ile Tyr Ser Lys
 245 250 255

Phe Asp Val Ile Asn Leu Ala Ala Glu Lys Thr Tyr Asn Asn Leu Asp
 260 265 270

Val Ser Val Thr Lys Ala Leu Gln His Arg Ser His Tyr Phe Glu Gly
 275 280 285

Val Leu Lys Cys Tyr Leu His Glu Thr Leu Glu Thr Ile Ile Asn Arg
 290 295 300

Leu Val Glu Ala Glu Val His Arg Leu Val Val Val Asp Glu Asn Asp
 305 310 315 320

Val Val Lys Gly Ile Val Ser Leu Ser Asp Ile Leu Gln Ala Leu Val
 325 330 335

Leu Thr Gly Gly Glu Lys Lys Pro
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<210> 462

<211> 85

<212> PRT

<213> Homo sapiens

<400> 462

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Asn Tyr Val Phe Tyr Ile Ser Ser Ser Leu Arg Leu Gly His Phe Ile
 20 25 30

Ser Val Asp Ile Ile Val Ser Ile Ile Leu Gln Asp Lys Lys His Leu

406

35 40 45
Leu Thr Thr Cys Gly Leu Lys Tyr Arg Pro Thr Leu Cys Ser Asn Ile
50 55 60
Met Leu Ile Ile Phe Leu Ala Val Leu His Ser Gly Gly Pro Asn Trp
65 70 75 80
Ile Arg Leu Leu His
85

<210> 463
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (45)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 463
Leu Ile Ser Cys Pro Met Glu Val Leu Ala Val Ser Ile Ser Leu Ile
1 5 10 15
Phe Val Ser Pro Asn Met Leu Val Gln Ile Arg Val Ser His Ile Phe
20 25 30
Leu Thr Ala Ser Asn Phe Tyr Leu Lys Trp Tyr Trp Xaa Leu Val Ser
35 40 45
Val Gln Asn Ile Leu
50

<210> 464
<211> 160
<212> PRT
<213> Homo sapiens

<400> 464
Gly Phe Thr Ala Ala Arg Arg Arg Gln Lys Gly Val Ser Gly Leu Leu
1 5 10 15
Leu Cys Gln Ala Gly Gly Val Leu Val Ser Ser Phe Val Met Ala Ala
20 25 30
Ala Val Ala Met Glu Thr Asp Asp Ala Gly Asn Arg Leu Arg Phe Gln

35 40 45
Leu Glu Leu Glu Phe Val Gln Cys Leu Ala Asn Pro Asn Tyr Leu Asn
50 55 60
Phe Leu Ala Gln Arg Gly Tyr Phe Lys Asp Lys Ala Phe Val Asn Tyr
65 70 75 80
Leu Lys Tyr Leu Leu Tyr Trp Lys Asp Pro Glu Tyr Ala Lys Tyr Leu
85 90 95
Lys Tyr Pro Gln Cys Leu His Met Leu Glu Leu Leu Gln Tyr Glu His
100 105 110
Phe Arg Lys Glu Leu Val Asn Ala Gln Cys Ala Lys Phe Ile Asp Glu
115 120 125
Gln Gln Ile Leu His Trp Gln His Tyr Ser Arg Lys Arg Met Arg Leu
130 135 140
Gln Gln Ala Leu Ala Glu Gln Gln Gln Gln Asn Asn Thr Ser Gly Lys
145 150 155 160

<210> 465
<211> 42
<212> PRT
<213> Homo sapiens

<400> 465
Ser Pro Ser Phe Leu Cys Ile Lys Val Ile Ile Ser Glu Glu His Arg
1 5 10 15
Asn Phe Ser Leu Phe Arg Glu Gly Lys Leu Ile Glu Asn Leu Ala Cys
20 25 30
Ser Thr Asn Lys Tyr Ser Cys Cys Lys Tyr
35 40

<210> 466
<211> 54
<212> PRT
<213> Homo sapiens

<400> 466

408

Arg Lys His Leu Glu Lys Met Thr His Trp Phe His Arg Asn Pro Leu
1 5 10 15
Lys Ala Thr Ala Pro Val Ser Phe Asn Tyr Tyr Gly Val Val Thr Gly
20 25 30
Pro Ser Ala Ser Lys Ile Cys Asn Asp Leu Arg Ser Ser Arg Ala Arg
35 40 45
Leu Leu Glu Thr Val His
50

<210> 467
<211> 49
<212> PRT
<213> Homo sapiens

<400> 467
Ala Asn Gly Gln Tyr Val Gln Leu Ala Cys Thr Ser Ser Thr Gly Leu
1 5 10 15
Val Val Trp Val Leu Leu Met Leu Gly Asn Ser Phe Cys His Asn His
20 25 30
Phe Thr Tyr Phe Phe Leu Tyr Cys Phe Ile Ile Ala Asn Ser Phe Ser
35 40 45
Leu

<210> 468
<211> 126
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 468
Xaa Gly Gly Gly Arg Cys Gln Val Pro Ala Ser His Arg Asn Gly Pro
1 5 10 15
Ala Gly Ala Gly Arg Leu Pro Thr Pro Thr Lys Glu Gly Ala Pro
20 25 30

Glu Ser Ala Cys Ala Ser Ile His Leu Ser Val Gln Ser Arg His Pro
 35 40 45

Cys Leu Ser Lys Ala Leu Thr Lys Thr Pro Ala Pro Gly Trp Pro Cys
 50 55 60

Ala Asp Leu Thr Gln Gly Met Phe Thr Trp Cys Ser Gly Arg Glu Gly
 65 70 75 80

Lys Gly Pro Gly Arg Gly His Gly Arg Arg Val Ala Ala Thr Arg Arg
 85 90 95

Arg Pro Gly Arg Pro Gly Thr Gln Ser Arg Met Thr Thr His Leu His
 100 105 110

Ala Thr Ala Ser Pro Glu Cys Ile Trp Asn Gln Ser Leu Asn
 115 120 125

<210> 469

<211> 76

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (70)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 469

Asp Arg Val Asn Arg Gly Met Pro Asp Val His Gly Phe Trp Gln Ser
 1 5 10 15

Arg Gly His Ile Ser Ile Ile Ala Met Leu Val Pro Pro Pro Ser Glu
 20 25 30

His Ser Gly Glu Gly Cys Glu Gly Ser Cys Asp Leu Asp Leu Arg Ser
 35 40 45

Pro Asp Arg Asn Leu Asp Ala Thr Gly Ser Arg Pro Gly Leu Arg Leu
 50 55 60

Gly Leu Val Asp Gly Xaa Leu Thr Val Phe Ala Asp
 65 70 75

<210> 470

<211> 193

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (52)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (154)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (167)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 470

Gly Pro Gly Leu Gly Gly Trp Ser Ser Ile Ser Ser Pro Arg Gly Cys
1 5 10 15

Arg Asp Ser Gly Arg Ser Val Ala Ala Ile Thr Asp Phe Leu Trp Asp
20 25 30

Lys Arg Thr Gly Leu Ala Ala Arg Thr Met Pro His Pro Arg Arg Tyr
35 40 45

His Ser Ser Xaa Arg Gly Ser Arg Gly Ser Tyr Arg Glu His Tyr Arg
50 55 60

Ser Arg Lys His Lys Arg Arg Arg Ser Arg Ser Trp Ser Ser Ser Ser
65 70 75 80

Asp Arg Thr Arg Arg Arg Arg Arg Glu Asp Ser Tyr His Val Arg Ser
85 90 95

Arg Ser Ser Tyr Asp Asp Arg Ser Ser Asp Arg Arg Val Tyr Asp Arg
100 105 110

Arg Tyr Cys Gly Ser Tyr Arg Arg Asn Asp Tyr Ser Arg Asp Arg Gly
115 120 125

Asp Ala Tyr Tyr Asp Thr Asp Tyr Arg His Ser Tyr Glu Tyr Gln Arg
130 135 140

Glu Asn Ser Ser Tyr Arg Ser Gln Arg Xaa Ala Gly Glu Ala Gln Thr
145 150 155 160

Ala Glu Glu Ala His Gly Xaa Phe Ser Arg Ser Ser Ser Val Ser Ala
165 170 175

411

Ser Pro Gly Pro Ser Ser Pro His Ser Ser Ala Gly Pro Leu Gly Leu
 180 185 190

Trp

<210> 471

<211> 111

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (105)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 471

Pro Ala Pro Gly Arg Gly Pro Pro Met Ala Gly Ala Ala Pro Thr Thr
 1 5 10 15

Ala Phe Gly Gln Ala Val Ile Gly Pro Pro Gly Ser Gly Lys Thr Thr
 20 25 30

Tyr Cys Leu Gly Met Ser Glu Phe Leu Arg Ala Leu Gly Arg Arg Val
 35 40 45

Ala Val Val Asn Leu Asp Pro Ala Asn Glu Gly Leu Pro Tyr Glu Cys
 50 55 60

Ala Val Asp Val Gly Glu Leu Val Gly Leu Gly Asp Val Met Asp Ala
 65 70 75 80

Leu Arg Leu Gly Pro Asn Gly Gly Leu Leu Tyr Phe Met Glu Tyr Leu
 85 90 95

Glu Ala Asn Leu Asp Trp Leu Arg Xaa Lys Leu Glu Pro Leu Arg
 100 105 110

<210> 472

<211> 65

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> Xaa equals any of the naturally occurring L-amino acids

412

<220>

<221> SITE

<222> (63)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 472

Lys Glu Gly Glu Lys Ser Ala Thr Leu Val Leu Leu Phe Cys Val Tyr
 1 5 10 15

Asn Phe Leu Lys Lys Ile Cys Val Leu Leu Leu Ile Thr Thr Leu Val
 20 25 30

Cys Pro Ser Ala Phe Phe Phe Phe Xaa Lys Thr Gly Ser His Ser Ile
 35 40 45

Gly Gln Ala Gly Val Gln Trp Cys Asn His Ser Ser Leu Gln Xaa Cys
 50 55 60

Pro

65

<210> 473

<211> 283

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (182)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 473

Gly Arg Gly Gly Arg Gly Trp Trp Gly Phe Trp Thr Glu Pro Leu Arg
 1 5 10 15

Val Arg Ala Asp Pro Val Ser Gly Cys Gly Gly Lys Met Ala Glu Leu
 20 25 30

Arg Val Leu Val Ala Val Lys Arg Val Ile Asp Tyr Ala Val Lys Ile
 35 40 45

Arg Val Lys Pro Asp Arg Thr Gly Val Val Thr Asp Gly Val Lys His
 50 55 60

Ser Met Asn Pro Phe Cys Glu Ile Ala Val Glu Glu Ala Val Arg Leu
 65 70 75 80

Lys Glu Lys Lys Leu Val Lys Glu Val Ile Ala Val Ser Cys Gly Pro

413

85	90	95
Ala Gln Cys Gln Glu Thr Ile Arg Thr Ala Leu Ala Met Gly Ala Asp		
100	105	110
Arg Gly Ile His Val Glu Val Pro Pro Ala Glu Ala Glu Arg Leu Gly		
115	120	125
Pro Leu Gln Val Ala Arg Val Leu Ala Lys Leu Ala Glu Lys Glu Lys		
130	135	140
Val Asp Leu Val Leu Leu Gly Lys Gln Ala Ile Asp Asp Asp Cys Asn		
145	150	155
Gln Thr Gly Gln Met Thr Ala Gly Phe Leu Asp Trp Pro Gln Gly Thr		
165	170	175
Phe Ala Ser Gln Val Xaa Leu Glu Gly Asp Lys Leu Lys Val Glu Arg		
180	185	190
Glu Ile Asp Gly Gly Leu Glu Thr Leu Arg Leu Lys Leu Pro Ala Val		
195	200	205
Val Thr Ala Asp Leu Arg Leu Asn Glu Pro Arg Tyr Ala Thr Leu Pro		
210	215	220
Asn Ile Met Lys Ala Lys Lys Lys Lys Ile Glu Val Ile Lys Pro Gly		
225	230	235
Asp Leu Gly Val Asp Leu Thr Ser Lys Leu Ser Val Ile Ser Val Glu		
245	250	255
Asp Pro Pro Gln Arg Thr Ala Gly Val Lys Val Glu Thr Thr Glu Asp		
260	265	270
Leu Val Ala Lys Leu Lys Glu Ile Gly Arg Ile		
275	280	

<210> 474

<211> 521

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (54)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (199)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (272)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 474

Cys Leu Thr Lys Leu Leu Pro Cys Phe Leu Glu His Asn Met Lys Arg
 1 5 10 15

Asp Glu Asp Leu His Lys Ala Ala Lys Glu Met Pro Phe Gln Gly Ser
 20 25 30

Gly Lys Ser Ala Trp Cys Pro Val Glu Ile Ser Lys Thr Val Leu Trp
 35 40 45

Pro Glu Ser Ile Ser Xaa Val Arg Cys Val Glu Leu Phe Glu Ala Pro
 50 55 60

Val Glu Cys Glu Glu Glu Glu Glu Val Glu Glu Glu Lys Gly Ser Phe
 65 70 75 80

Cys Ala Ser Pro Glu Ser Ser Arg Asp Asp Phe Gln Glu Gly Arg Glu
 85 90 95

Gly Ile Val Ala Arg Leu Thr Glu Ser Leu Phe Leu Asp Leu Leu Gly
 100 105 110

Glu Glu Asn Gly Gly Phe Cys Gln Gln Asp Met Gly Glu Ser Cys Leu
 115 120 125

Leu Pro Pro Ser Gly Ser Thr Ser Ala His Met Pro Trp Asp Glu Phe
 130 135 140

Pro Ser Ala Gly Pro Lys Glu Ala Pro Pro Trp Gly Lys Glu Gln Pro
 145 150 155 160

Leu His Leu Glu Pro Ser Pro Pro Ala Ser Pro Thr Gln Ser Pro Asp
 165 170 175

Asn Leu Thr Cys Thr Glu Thr Pro Leu Val Ile Ala Gly Asn Pro Ala
 180 185 190

Tyr Arg Ser Phe Ser Asn Xaa Leu Ser Gln Ser Pro Cys Pro Arg Glu
 195 200 205

Leu Gly Pro Asp Pro Leu Leu Ala Arg His Leu Glu Glu Val Glu Pro
 210 215 220

Glu Met Pro Cys Val Pro Gln Leu Ser Glu Pro Thr Thr Val Pro Gln
 225 230 235 240
 Pro Glu Pro Glu Thr Trp Glu Gln Ile Leu Arg Arg Asn Val Leu Gln
 245 250 255
 His Gly Ala Ala Ala Ala Pro Val Ser Ala Pro Thr Ser Gly Tyr Xaa
 260 265 270
 Glu Phe Val His Ala Val Glu Gln Gly Gly Thr Gln Ala Ser Ala Val
 275 280 285
 Val Gly Leu Gly Pro Pro Gly Glu Ala Gly Tyr Lys Ala Phe Ser Ser
 290 295 300
 Leu Leu Ala Ser Ser Ala Val Ser Pro Glu Lys Cys Gly Phe Gly Ala
 305 310 315 320
 Ser Ser Gly Glu Glu Gly Tyr Lys Pro Phe Gln Asp Leu Ile Pro Gly
 325 330 335
 Cys Pro Gly Asp Pro Ala Pro Val Pro Val Pro Leu Phe Thr Phe Gly
 340 345 350
 Leu Asp Arg Glu Pro Pro Arg Ser Pro Gln Ser Ser His Leu Pro Ser
 355 360 365
 Ser Ser Pro Glu His Leu Gly Leu Glu Pro Gly Glu Lys Val Glu Asp
 370 375 380
 Met Pro Lys Pro Pro Leu Pro Gln Glu Gln Ala Thr Asp Pro Leu Val
 385 390 395 400
 Asp Ser Leu Gly Ser Gly Ile Val Tyr Ser Ala Leu Thr Cys His Leu
 405 410 415
 Cys Gly His Leu Lys Gln Cys His Gly Gln Glu Asp Gly Gly Gln Thr
 420 425 430
 Pro Val Met Ala Ser Pro Cys Cys Gly Cys Cys Cys Gly Asp Arg Ser
 435 440 445
 Ser Pro Pro Thr Thr Pro Leu Arg Ala Pro Asp Pro Ser Pro Gly Gly
 450 455 460
 Val Pro Leu Glu Ala Ser Leu Cys Pro Ala Ser Leu Ala Pro Ser Gly
 465 470 475 480
 Ile Ser Glu Lys Ser Lys Ser Ser Ser Ser Phe His Pro Ala Pro Gly
 485 490 495

416

Asn Ala Gln Ser Ser Ser Gln Thr Pro Lys Ile Val Asn Phe Val Ser
 500 505 510

Val Gly Pro Thr Tyr Met Arg Val Ser
 515 520

<210> 475

<211> 245

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (163)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 475

Pro Val Ser Tyr His Pro Arg Met Cys Thr Gly Gly Cys Ala Arg Cys
 1 5 10 15

Leu Gly Gly Thr Leu Ile Pro Leu Ala Phe Phe Gly Phe Leu Ala Asn
 20 25 30

Ile Leu Leu Phe Phe Pro Gly Gly Lys Val Ile Asp Asp Asn Asp His
 35 40 45

Leu Ser Gln Glu Ile Trp Phe Phe Gly Gly Ile Leu Gly Ser Gly Val
 50 55 60

Leu Met Ile Phe Pro Ala Leu Val Phe Leu Gly Leu Lys Asn Asn Asp
 65 70 75 80

Cys Cys Gly Cys Cys Gly Asn Glu Gly Cys Gly Lys Arg Phe Ala Met
 85 90 95

Phe Thr Ser Thr Ile Phe Ala Val Val Gly Phe Leu Gly Ala Gly Tyr
 100 105 110

Ser Phe Ile Ile Ser Ala Ile Ser Ile Asn Lys Gly Pro Lys Cys Leu
 115 120 125

Met Ala Asn Ser Thr Trp Gly Tyr Pro Phe His Asp Gly Asp Tyr Leu
 130 135 140

Asn Asp Glu Ala Leu Trp Asn Lys Cys Arg Glu Pro Leu Asn Val Val
 145 150 155 160

Pro Trp Xaa Ser Asp Pro Leu Leu His Pro Ala Gly Arg Arg Arg Asn

[illegible]

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<210> 476
<211> 76
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids
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<400> 476
Met Ile Tyr His Pro Ala Phe Ile Lys Tyr Val Phe Asp Asn Trp Leu
  1             5             10             15
Gln Gly His Gly Arg Tyr Pro Ser Thr Gly Ile Leu Ser Val Ile Phe
      20             25             30
Ser Met His Val Cys Asp Glu Val Asp Leu Tyr Gly Phe Gly Ala Asp
      35             40             45
Ser Lys Gly Asn Trp Xaa Pro Leu Leu Gly Glu Gln Pro Ile Arg Gly
      50             55             60
Gly Phe Ser Gln Asp Gly Gly Ala Arg Cys Arg Leu
      65             70             75

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<210> 477
<211> 176
<212> PRT
<213> Homo sapiens
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<220>

<221> SITE

<222> (12)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (169)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 477

Ser	Gln	Phe	Arg	Met	Gly	Trp	Thr	Trp	Thr	Ala	Xaa	Ser	Leu	Ala	Pro
1				5					10					15	

Gln	Arg	Leu	Met	Ser	Val	Leu	Asn	Pro	Cys	Gln	Asn	Tyr	Thr	Leu	Leu
		20						25					30		

Asp	Glu	Pro	Phe	Arg	Ser	Thr	Glu	Asn	Ser	Ala	Gly	Ser	Gln	Gly	Cys
		35					40					45			

Asp	Lys	Asn	Met	Ser	Gly	Trp	Tyr	Arg	Phe	Val	Gly	Glu	Gly	Gly	Val
	50					55					60				

Arg	Met	Ser	Glu	Thr	Cys	Val	Gln	Val	His	Arg	Cys	Gln	Thr	Asp	Ala
65					70					75					80

Pro	Met	Trp	Leu	Asn	Gly	Thr	His	Pro	Ala	Leu	Gly	Asp	Gly	Ile	Thr
			85						90					95	

Asn	His	Thr	Ala	Cys	Ala	His	Trp	Ser	Gly	Asn	Cys	Cys	Phe	Trp	Lys
		100							105					110	

Thr	Glu	Val	Leu	Val	Lys	Ala	Cys	Pro	Gly	Gly	Tyr	His	Val	Tyr	Arg
		115					120						125		

Leu	Glu	Gly	Thr	Pro	Trp	Cys	Asn	Leu	Arg	Tyr	Cys	Thr	Asp	Pro	Ser
	130						135					140			

Thr	Val	Glu	Asp	Lys	Cys	Glu	Lys	Ala	Cys	Arg	Pro	Glu	Glu	Glu	Cys
145					150					155					160

Leu	Ala	Leu	Asn	Ser	Asn	Trp	Gly	Xaa	Phe	Cys	Arg	Gln	Gly	Pro	Gln
			165						170						175

<210> 478

419

<211> 97
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (72)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (96)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 478
 Met Arg Asp Ala Leu Leu Ala Tyr Ser Pro Gln Phe Thr Leu Ser Pro
 1 5 10 15
 Gln Val Ile Lys Tyr Gly Leu Lys Thr Gly Asn Val Ala Ser Leu Cys
 20 25 30
 Pro Trp Trp Ile Gly Pro Gln Ile Val Ile Leu Thr Thr Leu Thr Ala
 35 40 45
 Val Lys Val Glu Gly Ile Pro Ala Trp Ile His His Ser His Val Lys
 50 55 60
 Pro Ala Ala Pro Glu Thr Trp Xaa Ala Arg Pro Ser Pro Asp Asn Pro
 65 70 75 80
 Cys Arg Val Thr Leu Lys Met Met Thr Ser Pro Val Pro Val Thr Xaa
 85 90 95

Arg

<210> 479
 <211> 158
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (66)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 479
 Cys Asp Leu Ser Ser Arg Gln Arg Trp Asp Ile Met Ala Ser Ile Trp
 1 5 10 15

420

Val Gly His Arg Gly Thr Val Arg Asp Tyr Pro Asp Phe Ser Pro Ser
20 25 30

Val Asp Ala Glu Ala Ile Gln Lys Ala Ile Arg Gly Ile Gly Thr Asp
35 40 45

Glu Lys Met Leu Ile Ser Ile Leu Thr Glu Arg Ser Asn Ala Gln Arg
50 55 60

Gln Xaa Ile Val Lys Glu Tyr Gln Ala Ala Tyr Gly Lys Glu Leu Lys
65 70 75 80

Asp Asp Leu Lys Gly Asp Leu Ser Gly His Phe Glu His Leu Met Val
85 90 95

Ala Leu Val Thr Pro Pro Ala Val Phe Asp Ala Lys Gln Leu Lys Lys
100 105 110

Ser Met Lys Gly Ala Gly Thr Asn Glu Asp Ala Leu Ile Glu Ile Leu
115 120 125

Thr Thr Arg Thr Ser Arg Gln Met Lys Asp Ile Ser Gln Ala Tyr Leu
130 135 140

Tyr Ser Ile Gln Glu Glu Ser Trp Glu Met Asp Ile Ser Phe
145 150 155

<210> 480

<211> 105

<212> PRT

<213> Homo sapiens

<400> 480

Ile Tyr Cys Arg Met Leu Ile Phe Trp Thr Ile Thr Leu Phe Leu Leu
1 5 10 15

Gly Ala Ala Lys Gly Lys Glu Val Cys Tyr Glu Asp Leu Gly Cys Phe
20 25 30

Phe Asp Thr Glu Pro Trp Gly Gly Thr Ala Ile Arg Pro Leu Lys Ile
35 40 45

Leu Pro Trp Ser Pro Glu Lys Ile Gly Thr Arg Phe Leu Leu Tyr Thr
50 55 60

Asn Glu Asn Pro Asn Asn Phe Gln Ile Leu Leu Leu Ser Asp Pro Ser
65 70 75 80

421

Thr Ile Glu Ala Ser Asn Phe Gln Met Asp Arg Lys Thr Arg Phe Ile
 85 90 95

Ile His Gly Phe His Arg Gln Arg Gly
 100 105

<210> 481

<211> 136

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (17)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 481

Ile Arg Gln Arg Phe Gln Met Asp Arg Lys Thr Arg Phe Ile Ile His
 1 5 10 15

Xaa Phe Ile Asp Lys Gly Asp Glu Ser Trp Val Thr Asp Met Cys Lys
 20 25 30

Lys Leu Phe Glu Val Glu Glu Val Asn Cys Ile Cys Val Asp Trp Lys
 35 40 45

Lys Gly Ser Gln Ala Thr Tyr Thr Gln Ala Ala Asn Asn Val Arg Val
 50 55 60

Val Gly Ala Gln Val Ala Gln Met Leu Asp Ile Leu Leu Thr Glu Tyr
 65 70 75 80

Ser Tyr Pro Pro Ser Lys Val His Leu Ile Gly His Ser Leu Gly Ala
 85 90 95

His Val Ala Gly Glu Ala Gly Ser Lys Thr Pro Gly Leu Ser Arg Ile
 100 105 110

Thr Gly Leu Asp Pro Val Glu Ala Ser Phe Glu Ser Thr Pro Glu Glu
 115 120 125

Val Arg Leu Asp Pro Ser Glu Cys
 130 135

<210> 482

<211> 188

<212> PRT

422

<213> Homo sapiens

<220>

<221> SITE

<222> (124)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 482

Ala Ser Gln Val Glu Gly Ser Gln Gly Ala Glu Leu Leu Ser Glu Ile
1 5 10 15

Gln Ser Pro Gln Arg Asn Val Ser Phe Asp Val Leu Pro Ala Phe Asn
20 25 30

Ala Leu Gly Gln Leu Ser Ser Gly Ser Thr Pro Ser Pro Glu Val Tyr
35 40 45

Ala Gly Leu Ile Asp Leu Tyr Lys Ser Ser Asp Leu Pro Gly Gly Glu
50 55 60

Phe Ser Thr Cys Phe Thr Val Leu Gln Arg Asn Phe Ile Arg Ser Arg
65 70 75 80

Pro Thr Lys Leu Lys Asp Leu Ile Arg Leu Val Lys His Trp Tyr Lys
85 90 95

Glu Cys Glu Arg Lys Leu Lys Pro Lys Gly Ser Leu Pro Pro Lys Tyr
100 105 110

Ala Leu Glu Leu Leu Thr Ile Tyr Ala Trp Glu Xaa Gly Ser Gly Val
115 120 125

Pro Asp Phe Asp Thr Ala Glu Gly Phe Arg Thr Val Leu Glu Leu Val
130 135 140

Thr Gln Tyr Gln Gln Leu Cys Ile Phe Trp Lys Val Asn Tyr Asn Phe
145 150 155 160

Glu Asp Glu Thr Val Arg Lys Phe Leu Leu Ser Gln Leu Gln Lys Thr
165 170 175

Arg Pro Val Asp Leu Gly Pro Ser Arg Thr His Arg
180 185

<210> 483

<211> 78

<212> PRT

<213> Homo sapiens

423

<400> 483

Arg Arg Lys Val Ala Met Asp Leu Ile Pro Asn Leu Ala Val Glu Thr
 1 5 10 15

Trp Leu Leu Leu Ala Val Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr
 20 25 30

Arg Thr His Gly Leu Phe Lys Arg Leu Gly Ile Pro Gly Pro Thr Pro
 35 40 45

Leu Pro Leu Leu Gly Asn Val Leu Ser Tyr Arg Gln Gly Leu Trp Lys
 50 55 60

Phe Asp Thr Glu Cys Tyr Lys Lys Tyr Gly Lys Met Trp Gly
 65 70 75

<210> 484

<211> 211

<212> PRT

<213> Homo sapiens

<400> 484

Cys Thr Ser Ser Ala Pro Arg Arg Ser Ser Pro Cys Ser Ala Gly Pro
 1 5 10 15

Thr Trp Ser Gly Thr Leu Trp Arg Arg Arg Arg Arg Cys Trp Arg Thr
 20 25 30

Gly Cys Gly Ser Arg Ser Arg Cys Cys Gly Cys Ser Arg His Tyr Arg
 35 40 45

Thr Gly Ser Ala Val Pro Arg Glu Leu Leu Glu Lys Leu Ile Glu Ser
 50 55 60

Arg Gln Ala Asn Thr Gly Leu Phe Asn Leu Arg Gln Ile Val Leu Ala
 65 70 75 80

Lys Val Asp Gln Ala Leu His Thr Gln Thr Asp Ala Asp Pro Ala Glu
 85 90 95

Glu Tyr Ala Arg Leu Cys Gln Glu Ile Leu Gly Val Pro Ala Thr Pro
 100 105 110

Gly Thr Asn Met Pro Ala Thr Phe Gly His Leu Ala Gly Gly Tyr Asp
 115 120 125

Ala Gln Tyr Tyr Gly Tyr Leu Trp Ser Glu Val Tyr Ser Met Asp Met
 130 135 140

424

Phe His Thr Arg Phe Lys Gln Glu Gly Val Leu Asn Ser Lys Val Gly
 145 150 155 160
 Met Asp Tyr Arg Ser Cys Ile Leu Arg Pro Gly Gly Ser Glu Asp Ala
 165 170 175
 Ser Ala Met Leu Arg Arg Phe Leu Gly Arg Asp Pro Lys Gln Asp Ala
 180 185 190
 Phe Leu Leu Ser Lys Gly Leu Gln Val Gly Gly Cys Glu Pro Glu Pro
 195 200 205
 Gln Ser Gly
 210

<210> 485
 <211> 371
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (122)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 485
 Gly Ser Glu Lys Pro Gly Gly Ala Gly Trp Lys Glu Asp Glu Pro Thr
 1 5 10 15
 Lys Gln Arg Ser Glu Asp Ser Met Tyr Thr Ala Ile Pro Gln Ser Gly
 20 25 30
 Ser Pro Phe Pro Gly Ser Val Gln Asp Pro Gly Leu His Val Trp Arg
 35 40 45
 Val Glu Lys Leu Lys Pro Val Pro Val Ala Gln Glu Asn Gln Gly Val
 50 55 60
 Phe Phe Ser Gly Asp Ser Tyr Leu Val Leu His Asn Gly Pro Glu Glu
 65 70 75 80
 Val Ser His Leu His Leu Trp Ile Gly Gln Gln Ser Ser Arg Asp Glu
 85 90 95
 Gln Gly Ala Cys Ala Val Leu Ala Val His Leu Asn Thr Leu Leu Gly
 100 105 110
 Glu Arg Pro Val Gln His Arg Glu Val Xaa Gly Asn Glu Ser Asp Leu
 115 120 125

425

Phe Met Ser Tyr Phe Pro Arg Gly Leu Lys Tyr Gln Glu Gly Gly Val
130 135 140

Glu Ser Ala Phe His Lys Thr Ser Thr Gly Ala Pro Ala Ala Ile Lys
145 150 155 160

Lys Leu Tyr Gln Val Lys Gly Lys Lys Asn Ile Arg Ala Thr Glu Arg
165 170 175

Ala Leu Asn Trp Asp Ser Phe Asn Thr Gly Asp Cys Phe Ile Leu Asp
180 185 190

Leu Gly Gln Asn Ile Phe Ala Trp Cys Gly Gly Lys Ser Asn Ile Leu
195 200 205

Glu Arg Asn Lys Ala Arg Asp Leu Ala Leu Ala Ile Arg Asp Ser Glu
210 215 220

Arg Gln Gly Lys Ala Gln Val Glu Ile Val Thr Asp Gly Glu Glu Pro
225 230 235 240

Ala Glu Met Ile Gln Val Leu Gly Pro Lys Pro Ala Leu Lys Glu Gly
245 250 255

Asn Pro Glu Glu Asp Leu Thr Ala Asp Lys Ala Asn Ala Gln Ala Ala
260 265 270

Ala Leu Tyr Lys Val Ser Asp Ala Thr Gly Gln Met Asn Leu Thr Lys
275 280 285

Val Ala Asp Ser Ser Pro Phe Ala Leu Glu Leu Leu Ile Ser Asp Asp
290 295 300

Cys Phe Val Leu Asp Asn Gly Leu Cys Gly Lys Ile Tyr Ile Trp Lys
305 310 315 320

Gly Arg Lys Ala Asn Glu Lys Glu Arg Gln Ala Ala Leu Gln Val Ala
325 330 335

Glu Gly Phe Ile Ser Arg Met Gln Tyr Ala Pro Asn Thr Gln Val Glu
340 345 350

Ile Leu Pro Gln Gly Arg Glu Ser Pro Ile Phe Lys Gln Phe Phe Lys
355 360 365

Asp Trp Lys
370

<210> 486
<211> 61
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (23)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (53)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (61)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 486
Lys Gln His Phe Tyr Cys Leu Leu Pro Ala Asn Leu Tyr Leu Lys Pro
1 5 10 15
Leu Asp Thr Asp Ser Leu Xaa Trp Asp Phe Gly Ile Asp Gly Phe Leu
20 25 30
Pro Phe Phe Ser Ala Ser Ala Ser Ile Ala Phe Ile Lys Leu His Cys
35 40 45
Val Gln Lys Lys Xaa Xaa Lys Lys Lys Lys Gly Gly Xaa
50 55 60

<210> 487
<211> 198
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (151)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (180)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (195)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (198)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 487

Arg	Gly	Gly	Leu	Leu	Gly	Ala	Arg	Pro	Pro	Ala	Gln	Arg	Thr	Leu	Cys
1				5					10					15	

Cys	Pro	Ala	Arg	Cys	Gly	Cys	Cys	Trp	Arg	Ser	Trp	Pro	Ser	Pro	Arg
			20					25					30		

Arg	Ala	Ile	Gly	Ser	Ala	Glu	Ser	His	Trp	Cys	Tyr	Glu	Val	Gln	Ala
		35					40					45			

Glu	Ser	Ser	Asn	Tyr	Pro	Cys	Leu	Val	Pro	Val	Lys	Trp	Gly	Gly	Asn
	50					55					60				

Cys	Gln	Lys	Asp	Arg	Gln	Ser	Pro	Ile	Asn	Ile	Val	Thr	Thr	Lys	Ala
65					70					75					80

Lys	Val	Asp	Lys	Lys	Leu	Gly	Arg	Phe	Phe	Phe	Ser	Gly	Tyr	Asp	Lys
			85					90						95	

Lys	Gln	Thr	Trp	Thr	Val	Gln	Asn	Asn	Gly	His	Ser	Val	Met	Met	Leu
		100					105						110		

Leu	Glu	Asn	Lys	Ala	Ser	Ile	Ser	Gly	Gly	Gly	Leu	Pro	Ala	Pro	Tyr
		115					120					125			

Gln	Ala	Lys	Gln	Leu	His	Leu	His	Trp	Ser	Asp	Leu	Pro	Tyr	Lys	Gly
	130					135					140				

Ser	Glu	His	Ser	Leu	Asp	Xaa	Glu	Ala	Phe	Ala	Met	Gly	Asp	Ala	His
145				150					155					160	

Ser	Tyr	Met	Arg	Lys	Arg	Arg	Gly	His	Pro	Arg	Asn	Val	Lys	Glu	Ala
			165					170					175		

Gln	Asp	Pro	Xaa	Arg	Arg	Ile	Cys	Gly	Ala	Gly	Leu	Phe	Leu	Gly	Gly
		180					185						190		

Gly Trp Xaa Pro Gly Xaa
195

<210> 488

<211> 116

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (5)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (21)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (66)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (69)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 488

Lys Glu Gly Leu Xaa Ser Leu His Leu Leu Cys Ser Thr Ala His Tyr
1 5 10 15

Gln Lys Thr Ala Xaa Met Lys Ser Ile Tyr Phe Val Ala Gly Leu Phe
20 25 30

Val Met Leu Val Gln Gly Ser Trp Gln Arg Ser Leu Gln Asp Thr Glu
35 40 45

Glu Lys Ser Arg Ser Phe Ser Ala Ser Gln Ala Asp Pro Leu Ser Asp
50 55 60

Pro Xaa Gln Met Xaa Glu Asp Lys Arg His Ser Gln Gly Thr Phe Thr
65 70 75 80

Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val
85 90 95

Gln Trp Leu Met Asn Thr Lys Arg Asn Arg Asn Asn Ile Ala Lys Arg
100 105 110

His Gly Glu Phe
115

<210> 489
<211> 389
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (376)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (377)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (379)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 489
Val Trp Ser Phe Ser Leu Asp Thr Glu Pro Ser Arg Gln Ala Lys Gln
1 5 10 15

Ala Arg Thr His His Pro Ala Pro Gly Pro Ala Ser Leu Leu Pro Ser
20 25 30

Asn Ala Met Gly Ser Asn Leu Ser Pro Gln Leu Cys Leu Met Pro Phe
35 40 45

Ile Leu Gly Leu Leu Ser Gly Gly Val Thr Thr Thr Pro Trp Ser Leu
50 55 60

Ala Arg Pro Gln Gly Ser Cys Ser Leu Glu Gly Val Glu Ile Lys Gly
65 70 75 80

Gly Ser Phe Arg Leu Leu Gln Glu Gly Gln Ala Leu Glu Tyr Val Cys
85 90 95

Pro Ser Gly Phe Tyr Pro Tyr Pro Val Gln Thr Arg Thr Cys Arg Ser
100 105 110

Thr Gly Ser Trp Ser Thr Leu Lys Thr Gln Asp Gln Lys Thr Val Arg
115 120 125

430

Lys Ala Glu Cys Arg Ala Ile His Cys Pro Arg Pro His Asp Phe Glu
130 135 140

Asn Gly Glu Tyr Trp Pro Arg Ser Pro Tyr Tyr Asn Val Ser Asp Glu
145 150 155 160

Ile Ser Phe His Cys Tyr Asp Gly Tyr Thr Leu Arg Gly Ser Ala Asn
165 170 175

Arg Thr Cys Gln Val Asn Gly Arg Trp Ser Gly Gln Thr Ala Ile Cys
180 185 190

Asp Asn Gly Ala Gly Tyr Cys Ser Asn Pro Gly Ile Pro Ile Gly Thr
195 200 205

Arg Lys Val Gly Ser Gln Tyr Arg Leu Glu Asp Ser Val Thr Tyr His
210 215 220

Cys Ser Arg Gly Leu Thr Leu Arg Gly Ser Gln Arg Arg Thr Cys Gln
225 230 235 240

Glu Gly Gly Ser Trp Ser Gly Thr Glu Pro Ser Cys Gln Asp Ser Phe
245 250 255

Met Tyr Asp Thr Pro Gln Glu Val Ala Glu Ala Phe Leu Ser Ser Leu
260 265 270

Thr Glu Thr Ile Glu Gly Val Asp Ala Glu Asp Gly His Gly Pro Gly
275 280 285

Glu Gln Gln Lys Arg Lys Ile Val Leu Asp Pro Ser Gly Ser Met Asn
290 295 300

Ile Tyr Leu Val Leu Asp Gly Ser Asp Ser Ile Gly Ala Ser Asn Phe
305 310 315 320

Thr Gly Ala Lys Lys Cys Leu Val Asn Leu Ile Glu Lys Val Ala Ser
325 330 335

Tyr Gly Val Lys Pro Arg Tyr Gly Leu Val Thr Tyr Ala Thr Tyr Pro
340 345 350

Lys Ile Trp Val Lys Val Ser Glu Ala Asp Ser Ser Asn Ala Gly Leu
355 360 365

Gly His Gly Ser Ser Phe Asn Xaa Xaa Gln Xaa Leu Lys Thr Thr Ser
370 375 380

Leu Lys Ser Gly Ala
385

431

<210> 490
 <211> 187
 <212> PRT
 <213> Homo sapiens

<400> 490

Ala Leu Leu Glu Gly Leu Asp Tyr Tyr Thr Gly Val Ile Tyr Glu Ala
 1 5 10 15

Val Leu Leu Gln Thr Pro Ala Gln Ala Gly Glu Glu Pro Leu Gly Val
 20 25 30

Gly Ser Val Ala Ala Gly Gly Arg Tyr Asp Gly Leu Val Gly Met Phe
 35 40 45

Asp Pro Lys Gly Arg Lys Val Pro Cys Val Gly Leu Ser Ile Gly Val
 50 55 60

Glu Arg Ile Phe Ser Ile Val Glu Gln Arg Leu Glu Ala Leu Glu Glu
 65 70 75 80

Lys Ile Arg Thr Thr Glu Thr Gln Val Leu Val Ala Ser Ala Gln Lys
 85 90 95

Lys Leu Leu Glu Glu Arg Leu Lys Leu Val Ser Glu Leu Trp Asp Ala
 100 105 110

Gly Ile Lys Ala Glu Leu Leu Tyr Lys Lys Asn Pro Lys Leu Leu Asn
 115 120 125

Gln Leu Gln Tyr Cys Glu Glu Ala Gly Ile Pro Leu Val Ala Ile Ile
 130 135 140

Gly Glu Gln Glu Leu Lys Asp Gly Val Ile Lys Leu Arg Ser Val Thr
 145 150 155 160

Ser Arg Glu Glu Val Asp Val Arg Arg Glu Asp Leu Val Glu Glu Ile
 165 170 175

Lys Arg Arg Thr Gly Gln Pro Leu Cys Ile Cys
 180 185

<210> 491
 <211> 271
 <212> PRT
 <213> Homo sapiens

432

<400> 491

Gln Tyr Lys Arg His Cys Ile Asn Cys Leu His Val Val Thr Leu Tyr
 1 5 10 15

Asn Arg Ile Lys Arg Asp Pro Ala Lys Ala Phe Val Pro Arg Thr Val
 20 25 30

Met Ile Gly Gly Lys Ala Ala Pro Gly Tyr His Met Ala Lys Leu Ile
 35 40 45

Ile Lys Leu Val Thr Ser Ile Gly Asp Val Val Asn His Asp Pro Val
 50 55 60

Val Gly Asp Arg Leu Lys Val Ile Phe Leu Glu Asn Tyr Arg Val Ser
 65 70 75 80

Leu Ala Glu Lys Val Ile Pro Ala Ala Asp Leu Ser Gln Gln Ile Ser
 85 90 95

Thr Ala Gly Thr Glu Ala Ser Gly Thr Gly Asn Met Lys Phe Met Leu
 100 105 110

Asn Gly Ala Leu Thr Ile Gly Thr Met Asp Gly Ala Asn Val Glu Met
 115 120 125

Ala Glu Glu Ala Gly Ala Glu Asn Leu Phe Ile Phe Gly Leu Arg Val
 130 135 140

Glu Asp Val Glu Ala Leu Asp Arg Lys Gly Tyr Asn Ala Arg Glu Tyr
 145 150 155 160

Tyr Asp His Leu Pro Glu Leu Lys Gln Ala Val Asp Gln Ile Ser Ser
 165 170 175

Gly Phe Phe Ser Pro Lys Glu Pro Asp Cys Phe Lys Asp Ile Val Asn
 180 185 190

Met Leu Met His His Asp Arg Phe Lys Val Phe Ala Asp Tyr Glu Ala
 195 200 205

Tyr Met Gln Cys Gln Ala Gln Val Asp Gln Leu Tyr Arg Asn Pro Lys
 210 215 220

Glu Trp Thr Lys Lys Val Ile Arg Asn Ile Ala Cys Ser Gly Lys Phe
 225 230 235 240

Ser Ser Asp Arg Thr Ile Thr Glu Tyr Ala Arg Glu Ile Trp Gly Val
 245 250 255

Glu Pro Ser Asp Leu Gln Ile Pro Pro Pro Asn Ile Pro Arg Asp
 260 265 270

<210> 492
 <211> 147
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (100)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (128)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (130)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (132)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (133)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (139)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (143)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 492
 Ser Thr His Ala Ser Glu Arg Gln Ser His Gln Leu Pro Leu Val Gly
 1 5 10 15

Leu Leu L u Phe Ser Phe Ile Pro Ser Gln Leu Cys Glu Ile Cys Glu
 20 25 30

Val Ser Glu Glu Asn Tyr Ile Arg Leu Lys Pro Leu Leu Asn Thr Met

35 40 45
 Ile Gln Ser Asn Tyr Asn Arg Gly Thr Ser Ala Val Asn Val Val Leu
 50 55 60
 Ser Leu Lys Leu Val Gly Ile Gln Ile Gln Thr Leu Met Gln Lys Met
 65 70 75 80
 Ile Gln Gln Ile Lys Tyr Asn Val Lys Ser Arg Leu Ser Asp Val Ser
 85 90 95
 Ser Gly Glu Xaa Ala Leu Ile Ile Leu Ala Leu Gly Val Cys Arg Asn
 100 105 110
 Ala Glu Glu Asn Leu Ile Tyr Asp Tyr His Leu Ile Asp Lys Leu Xaa
 115 120 125
 Asn Xaa Ile Xaa Xaa Gln Lys Leu Glu Asn Xaa Gly Gly Thr Xaa Trp
 130 135 140
 Ala Leu Pro
 145

<210> 493

<211> 161

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (152)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 493

Leu Asp Phe Asn Leu Thr Asp Pro Glu Asn Gly Pro Val Leu Asp Asp
 1 5 10 15
 Ser Leu Pro Asn Ser Val His Glu Tyr Ile Pro Phe Ala Lys Asp Cys
 20 25 30
 Gly Asn Lys Glu Lys Cys Ile Ser Asp Leu Ser Leu His Val Ala Thr
 35 40 45
 Thr Glu Lys Asp Leu Leu Ile Val Arg Ser Gln Asn Asp Lys Phe Asn
 50 55 60
 Val Ser Leu Thr Val Lys Asn Thr Lys Asp Ser Ala Tyr Asn Thr Arg
 65 70 75 80

Thr Ile Val His Tyr Ser Pro Asn Leu Val Phe Ser Gly Ile Glu Ala
85 90 95
Ile Gln Lys Asp Ser Cys Glu Ser Asn His Asn Ile Thr Cys Lys Val
100 105 110
Gly Tyr Pro Phe Leu Arg Arg Gly Glu Met Val Thr Phe Lys Ile Leu
115 120 125
Phe Gln Phe Asn Thr Ser Tyr Leu Met Gly Lys Cys Asp His Leu Phe
130 135 140
Lys Cys Thr Ser Gly Gln Arg Xaa Asn Leu Leu Lys Pro Phe Leu Ile
145 150 155 160
Met

<210> 494
<211> 139
<212> PRT
<213> Homo sapiens

<400> 494
Val Glu Thr Gly Trp Val Glu Leu Pro Glu Val Leu Ala Pro Ser Ser
1 5 10 15
Arg Arg Ala Phe Pro Ile Leu His Gly Ala Leu His Leu Asp Gln Gln
20 25 30
Ser Pro Gly Val Glu Ala Ser Asp Trp Arg Gly Trp Arg Gly Ala His
35 40 45
His Leu Cys Cys Gly Pro Gly Ile Met Ser Lys Leu Trp Leu Gly Phe
50 55 60
Asp Leu Arg Ala Ala Ile Ala Ala Pro Ile Leu His Val Asn Ser Lys
65 70 75 80
Gly Cys Val Glu Tyr Glu Pro Asn Phe Ser Gln Glu Val Gln Arg Gly
85 90 95
Leu Gln Asp Arg Gly Gln Asn Gln Thr Gln Arg Pro Phe Phe Leu Asn
100 105 110
Val Val Gln Ala Val Ser Gln Glu Gly Ala Cys Val Tyr Ala Val Ser
115 120 125
Asp Leu Arg Lys Ser Gly Glu Ala Ala Gly Tyr

130

135

<210> 495

<211> 215

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (139)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 495

Ala Ser His Ser Arg Gly Ser Ser Ser Ser Ser His Ser Ser Ser Val
 1 5 10 15

Arg Arg Gly Ser Ser Tyr Ser Ser Ser Met Ser Thr Gly Gly Gly Gly
 20 25 30

Ala Gly Ser Leu Gly Ala Gly Gly Ala Phe Gly Glu Ala Ala Gly Asp
 35 40 45

Arg Gly Pro Tyr Gly Thr Asp Ile Gly Pro Gly Gly Gly Tyr Gly Ala
 50 55 60

Ala Ala Glu Gly Gly Met Tyr Ala Gly Asn Gly Gly Leu Leu Gly Ala
 65 70 75 80

Asp Phe Ala Gly Asp Leu Asp Tyr Asn Glu Leu Ala Val Arg Val Ser
 85 90 95

Glu Ser Met Gln Arg Gln Gly Leu Leu Gln Gly Met Ala Tyr Thr Val
 100 105 110

Gln Gly Pro Pro Gly Gln Pro Gly Pro Gln Gly Pro Pro Gly Ile Ser
 115 120 125

Lys Val Phe Ser Ala Tyr Ser Asn Val Thr Xaa Asp Leu Met Asp Phe
 130 135 140

Phe Gln Thr Tyr Gly Ala Ile Gln Gly Pro Pro Gly Gln Lys Gly Glu
 145 150 155 160

Met Gly Thr Pro Gly Pro Lys Gly Asp Arg Gly Pro Ala Gly Pro Pro
 165 170 175

Gly His Pro Gly Pro Pro Gly Pro Ser Arg Thr Gln Gly Arg Lys Arg
 180 185 190

Arg Gln Arg Leu Thr Lys Ser Met Leu Gly Gly Glu Gly Glu Glu Val
 195 200 205

Ile Gly Cys Gln Pro Leu Ser
 210 215

<210> 496

<211> 309

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (247)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 496

Pro Pro Gly Ile Pro Gly Gln Pro Gly Leu Lys Gly Leu Pro Gly Pro
 1 5 10 15

Gln Gly Pro Gln Gly Leu Pro Gly Pro Thr Gly Pro Pro Gly Asp Pro
 20 25 30

Gly Arg Asn Gly Leu Pro Gly Phe Asp Gly Ala Gly Gly Arg Lys Gly
 35 40 45

Asp Pro Gly Leu Pro Gly Gln Pro Gly Thr Arg Gly Leu Asp Gly Pro
 50 55 60

Pro Gly Pro Asp Gly Leu Gln Gly Pro Pro Gly Pro Pro Gly Thr Ser
 65 70 75 80

Ser Val Ala His Gly Phe Leu Ile Thr Arg His Ser Gln Thr Thr Asp
 85 90 95

Ala Pro Gln Cys Pro Gln Gly Thr Leu Gln Val Tyr Glu Gly Phe Ser
 100 105 110

Leu Leu Tyr Val Gln Gly Asn Lys Arg Ala His Gly Gln Asp Leu Gly
 115 120 125

Thr Ala Gly Ser Cys Leu Arg Arg Phe Ser Thr Met Pro Phe Met Phe
 130 135 140

Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser
 145 150 155 160

Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met Gln Pro Leu
 165 170 175

Lys Gly Gln Ser Ile Gln Pro Phe Ile Ser Arg Cys Ala Val Cys Glu
 180 185 190
 Ala Pro Ala Val Val Ile Ala Val His Ser Gln Thr Ile Gln Ile Pro
 195 200 205
 His Cys Pro Gln Gly Trp Asp Ser Leu Trp Ile Gly Tyr Ser Phe Met
 210 215 220
 Met His Thr Ser Ala Gly Ala Glu Gly Ser Gly Gln Ala Leu Ala Ser
 225 230 235 240
 Pro Gly Ser Cys Leu Glu Xaa Phe Arg Ser Ala Pro Phe Ile Glu Cys
 245 250 255
 His Gly Arg Gly Thr Cys Asn Tyr Tyr Ala Asn Ser Tyr Ser Phe Trp
 260 265 270
 Leu Ala Thr Val Asp Val Ser Asp Met Phe Ser Lys Pro Gln Ser Glu
 275 280 285
 Thr Leu Lys Ala Gly Asp Leu Arg Thr Arg Ile Ser Arg Cys Gln Val
 290 295 300
 Cys Met Lys Arg Thr
 305

<210> 497
 <211> 40
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (38)
 <223> xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (40)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 497
 Thr Leu Cys Tyr Cys Ser Ser Gln Met Leu Phe Tyr Ile Cys Lys Lys
 1 5 10 15
 Leu Thr Ser His Gln Met Leu Ser Ser Thr Glu Ile Leu Lys Trp Leu
 20 25 30

Arg Gly Asn Ile Asp Xaa Gln Xaa
35 40

<210> 498
<211> 88
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 498
Cys Pro Arg Ser Leu Xaa Tyr Phe Arg Met Tyr Ala Lys Glu Phe Asp
1 5 10 15

Leu Leu Lys Tyr Ile Arg Phe Lys Thr Thr Val Cys Ser Val Lys Lys
20 25 30

Gln Pro Asp Phe Ala Thr Ser Gly Gln Trp Glu Val Val Thr Glu Ser
35 40 45

Glu Gly Lys Lys Glu Met Asn Val Phe Asp Gly Val Met Val Cys Thr
50 55 60

Gly His His Thr Asn Ala His Leu Pro Leu Glu Ser Phe Pro Gly Glu
65 70 75 80

Gln Leu Thr Arg Lys Glu Asp Pro
85

<210> 499
<211> 253
<212> PRT
<213> Homo sapiens

<400> 499
Leu Arg Trp Leu Pro Ala Ala Ser Thr Ser Leu Ala Ala Leu Ala Thr
1 5 10 15

Leu Ala Asp Cys Cys Ala Ala Gly Ala Met Ser Val Ser Glu Ile Phe
20 25 30

Val Glu Leu Gln Gly Phe Leu Ala Ala Glu Gln Asp Ile Arg Glu Glu
35 40 45

440

Ile Arg Lys Val Val Gln Ser Leu Glu Gln Thr Ala Arg Glu Ile Leu
 50 55 60
 Thr Leu Leu Gln Gly Val His Gln Gly Ala Gly Phe Gln Asp Ile Pro
 65 70 75 80
 Lys Arg Cys Leu Lys Ala Arg Glu His Phe Gly Thr Val Lys Thr His
 85 90 95
 Leu Thr Ser Leu Lys Thr Lys Phe Pro Ala Glu Gln Tyr Tyr Arg Phe
 100 105 110
 His Glu His Trp Arg Phe Val Leu Gln Arg Leu Val Phe Leu Ala Ala
 115 120 125
 Phe Val Val Tyr Leu Glu Thr Glu Thr Leu Val Thr Arg Glu Ala Val
 130 135 140
 Thr Glu Ile Leu Gly Ile Glu Pro Asp Arg Glu Lys Gly Phe His Leu
 145 150 155 160
 Asp Val Glu Asp Tyr Leu Ser Gly Val Leu Ile Leu Ala Ser Glu Leu
 165 170 175
 Ser Arg Leu Ser Val Asn Ser Val Thr Ala Gly Asp Tyr Ser Arg Pro
 180 185 190
 Leu His Ile Ser Thr Phe Ile Asn Glu Leu Asp Ser Gly Phe Arg Leu
 195 200 205
 Leu Asn Leu Lys Asn Asp Ser Leu Arg Lys Arg Tyr Asp Gly Leu Lys
 210 215 220
 Tyr Asp Val Lys Lys Val Glu Glu Val Val Tyr Asp Leu Ser Ile Arg
 225 230 235 240
 Gly Phe Asn Lys Glu Thr Ala Ala Ala Cys Val Glu Lys
 245 250

<210> 500

<211> 169

<212> PRT

<213> Homo sapiens

<400> 500

Arg Thr Arg Gly Arg Thr Arg Gly Leu Glu Phe Gly Leu Gln Pro His
 1 5 10 15

441

Lys Ile Pro Asp Thr Glu Thr Leu Cys Tyr Val Met Pro Ser Ser Ser
20 25 30

Ala Arg Cys Ala Gln Phe Pro Arg Ala Gln Asp Lys Val His Tyr Tyr
35 40 45

Ile Lys Leu Lys Asp Leu Arg Asp Gln Leu Lys Gly Ile Glu Arg Asn
50 55 60

Met Asp Val Gln Glu Val Gln Tyr Thr Phe Asp Leu Gln Leu Ala Gln
65 70 75 80

Glu Asp Ala Lys Lys Met Ala Val Lys Glu Glu Lys Tyr Asp Pro Gly
85 90 95

Tyr Glu Ala Ala Tyr Gly Gly Ala Tyr Gly Glu Asn Pro Cys Ser Ser
100 105 110

Glu Pro Cys Gly Phe Ser Ser Asn Gly Leu Ile Glu Ser Val Glu Leu
115 120 125

Arg Gly Glu Ser Ala Phe Ser Gly Ile Pro Asn Gly Gln Trp Met Thr
130 135 140

Gln Ser Phe Thr Asp Gln Ile Pro Ser Phe Ser Asn His Cys Gly Thr
145 150 155 160

Gln Glu Gln Glu Glu Glu Ser His Ala
165

<210> 501

<211> 119

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (16)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (54)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (55)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (83)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (88)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (97)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (99)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (101)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (117)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 501
 Gly His Xaa Ala Arg Gln Gly His Leu Ser Ser Pro Thr Asp Gly Xaa
 1 5 10 15
 Arg Gln Gly His Ser Gln Phe Trp Glu Val Ile Ser Asp Glu His Ala
 20 25 30
 Ile Asp Ser Ala Gly Thr Tyr His Gly Asp Ser His Leu Gln Leu Glu
 35 40 45
 Arg Ile Asn Val Tyr Xaa Xaa Glu Ala Ser Gly Gly Arg Tyr Val Pro
 50 55 60
 Arg Ala Val Leu Val Asp Leu Glu Pro Gly Thr Met Asp Ser Val Arg
 65 70 75 80

Ser Gly Xaa Phe Gly Gln Val Xaa Arg Pro Asp Asn Phe Ile Phe Gly
85 90 95

Xaa Leu Xaa Ala Xaa Thr Gly Val Arg Leu Leu Ser Gln Gly Ser Ser
100 105 110

Lys Ser Arg Asn Xaa Pro Arg
115

<210> 502

<211> 112

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (30)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (43)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (54)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (103)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (109)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (110)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 502

Thr His Leu Trp Lys Arg Asn Pro Cys Asp Cys Gly Thr Lys Lys Ser
1 5 10 15

444

Ala Ser Tyr Gln Thr Ile Arg Phe Cys His Glu Lys Trp Xaa Lys Cys
 20 25 30

Arg Leu Ser Gly Glu Gly Phe Tyr Pro Lys Xaa Ile Arg Ile Asn Leu
 35 40 45

Val Ser Ser Lys Lys Xaa Thr Glu Phe Asp Pro Ala Ile Val Ile Ser
 50 55 60

Pro Ser Gly Lys Tyr Asn Ala Val Asn Leu Gly Lys Tyr Glu Asp Ser
 65 70 75 80

Asn Ser Val Thr Cys Ser Val Gln His Asp Asn Lys Thr Val His Ser
 85 90 95

Thr Asp Phe Gly Ser Glu Xaa Arg Phe Tyr Arg Ser Xaa Xaa Thr Lys
 100 105 110

<210> 503

<211> 156

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (32)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (137)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 503

Asp Ser Ser His Arg Ser Arg Arg His His Arg Ala Ser Ala Ser Ala
 1 5 10 15

Ala Ala Ala Ala Ala Pro Gly Pro Arg Pro Phe Ala Ala Leu Val Xaa
 20 25 30

Pro Ala Leu Leu Arg Arg Arg Leu Pro Pro Arg Pro Ala Met Pro Leu
 35 40 45

Tyr Ser Val Thr Val Lys Trp Gly Lys Glu Lys Phe Glu Gly Val Glu
 50 55 60

Leu Asn Thr Asp Glu Pro Pro Met Val Phe Lys Ala Gln Leu Phe Ala
65 70 75 80

Leu Thr Gly Val Gln Pro Ala Arg Gln Lys Val Met Val Lys Gly Gly
85 90 95

Thr Leu Lys Asp Asp Asp Trp Gly Asn Ile Lys Ile Lys Asn Gly Met
100 105 110

Thr Leu Leu Met Met Gly Ser Ala Asp Ala Leu Pro Glu Glu Pro Ser
115 120 125

Ala Lys Thr Val Phe Val Glu Asp Xaa Asp Arg Arg Thr Val Ser Ile
130 135 140

Cys Tyr Gly Val Thr Met Trp Ile Asp Lys Pro Trp
145 150 155

<210> 504

<211> 155

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (8)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (104)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (117)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (154)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 504

Val Phe Lys Glu Gln Glu Leu Xaa Pro Glu Asp Lys Gly Ala Val Pro
1 5 10 15

Glu Asp Ala Ser Thr Glu Arg Ser Ala Met Ala Ser Leu Gly Leu Gln
20 25 30

Leu Val Gly Tyr Ile Leu Gly Leu Leu Gly Leu Leu Gly Thr Leu Val
 35 40 45
 Ala Met Leu Leu Pro Ser Trp Lys Thr Ser Ser Tyr Val Gly Ala Ser
 50 55 60
 Ile Val Thr Ala Val Gly Phe Ser Lys Gly Leu Trp Met Glu Cys Ala
 65 70 75 80
 Thr His Ser Thr Gly Ile Thr Gln Cys Asp Ile Tyr Ser Thr Leu Leu
 85 90 95
 Gly Leu Pro Ala Asp Ile Gln Xaa Ala Gln Ala Met Met Val Thr Ser
 100 105 110
 Ser Ala Ile Ser Xaa Leu Ala Cys Ile Ile Ser Val Val Gly Met Arg
 115 120 125
 Cys Thr Val Phe Cys Gln Glu Ser Arg Ala Lys Asp Arg Val Ala Val
 130 135 140
 Ala Gly Gly Val Phe Phe Ile Leu Gly Xaa Leu
 145 150 155

<210> 505

<211> 120

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (76)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 505

Ser Asp His Pro Pro Pro Pro Ala Leu His Gln Ala Thr Gly Leu Gly
 1 5 10 15
 Phe Leu Leu Ile Thr Ile Cys Cys Tyr His Gly Thr Gln Gln Gly Ile
 20 25 30
 Pro Gly Pro Pro Ala Lys Trp Leu Pro Lys Ser Pro Leu Leu Thr Gln
 35 40 45
 Lys Ser Gly Met Ala Leu Lys Arg Cys Lys Phe Leu Tyr Cys Tyr Pro
 50 55 60
 Pro His His Gln Asp His Val Gly Cys Ser Leu Xaa Ser Leu Thr Arg

447

[illegible]

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<210> 506
<211> 102
<212> PRT
<213> Homo sapiens
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<220>
<221> SITE
<222> (45)
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>  
<221> SITE  
<222> (80)  
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (92)
<223> Xaa equals any of the naturally occurring L-amino acids
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<400> 506
Pro Phe Gln Pro Pro Leu Leu Asp Leu Arg Arg Pro Ser Gln Gln Ser
1 5 10 15

Gln Trp Pro Gln His Leu Ala Gly Gln Leu Pro Ser Leu Leu Ile Cys
20 25 30

Gln Thr Arg Thr Gln Thr Lys Pro Met Arg Asn Gly Xaa Thr Ala Ser
35 40 45

Glu Ser Ser Asp Phe Thr Ser Glu Arg Arg Gly Asp Lys Glu Ala Pro
50 55 60

Pro	Pro	Val	Leu	Leu	Thr	Pro	Lys	Ala	Val	Gly	Thr	Pro	Gly	Gly	Xaa
65					70					75					80

Gly Gly Gly Ala Leu Pro Gly Ile Ser Ala Met Xaa Arg Gly Asp Leu
85 90 95

Ser Gln Arg Ala Lys Ile
100

<210> 507

<211> 103

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (68)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 507

Cys Gln Gln Leu Ile Tyr Glu Pro Thr Ile Val Pro His Cys Thr Lys
1 5 10 15

Val Ser His Lys Arg Asn Arg Ile Phe Trp Ser Thr Asp Cys Ser Arg
20 25 30

Val Ala Pro Leu Cys Ala Ala Gly Val Val Val Phe Ile Phe Met Val
35 40 45

Arg Phe Asn Ile Asn Tyr Leu Ser Cys His Ala Phe Phe Phe Leu Gln
50 55 60

Phe Ser Arg Xaa Ser Thr Glu Gln Phe Leu Ile Ser Tyr Leu Glu Tyr
65 70 75 80

Glu Ser Arg Phe Tyr Phe Val Met Leu Ile Ile Pro Lys Asp Ala Leu
85 90 95

Asn Ala Trp Lys Asn Ala Phe
100

<210> 508

<211> 51

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (32)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (36)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 508

Glu Pro Pro Leu Ile Val Ser Ser Phe Ser Gly Gln Glu Ala Gln Thr
 1 5 10 15

Glu Leu Pro Gln Ala Arg Ile Ser Cys Pro Glu Gly Thr Asn Ala Xaa
 20 25 30

Arg Ser Tyr Xaa Tyr Tyr Phe Asn Gly Arg Pro Trp Arg Pro Gly Leu
 35 40 45

Met Gln Met
 50

<210> 509

<211> 73

<212> PRT

<213> Homo sapiens

<400> 509

Ile Phe Leu Tyr Phe Thr Trp Ala Ser Leu Tyr Thr Ala Ile Tyr Thr
 1 5 10 15

Ile Ile Ser Tyr Ser Tyr Met Phe Phe Val Pro Phe Val Val Leu Phe
 20 25 30

Val Leu Leu Asp Ser Tyr Leu Asp Gly Asn Ala Leu Ser Gly Phe Gly
 35 40 45

Cys Phe Ser Cys Phe Ser Ile Cys Ile Lys Lys Leu Val His Val Asn
 50 55 60

Thr Phe His Val Phe Ser Ser Asn Val
 65 70

<210> 510

<211> 218

<212> PRT

<213> Homo sapiens

<400> 510

Glu Thr Arg Val Pro Ala Arg Pro Gly Gln Ala Arg Ala Met Glu Phe
 1 5 10 15

450

Leu Trp Ala Pro Leu Leu Gly Leu Cys Cys Ser Leu Ala Ala Ala Asp
 20 25 30
 Arg His Thr Val Phe Trp Asn Ser Ser Asn Pro Lys Phe Arg Asn Glu
 35 40 45
 Asp Tyr Thr Ile His Val Gln Leu Asn Asp Tyr Val Asp Ile Ile Cys
 50 55 60
 Pro His Tyr Glu Asp His Ser Val Ala Asp Ala Ala Met Glu Gln Tyr
 65 70 75 80
 Ile Leu Tyr Leu Val Glu His Glu Glu Tyr Gln Leu Cys Gln Pro Gln
 85 90 95
 Ser Lys Asp Gln Val Arg Trp Gln Cys Asn Arg Pro Ser Ala Lys His
 100 105 110
 Gly Pro Glu Lys Leu Ser Glu Lys Phe Gln Arg Phe Thr Pro Phe Thr
 115 120 125
 Leu Gly Lys Glu Phe Lys Glu Gly His Ser Tyr Tyr Tyr Ile Ser Lys
 130 135 140
 Pro Ile His Gln His Glu Asp Arg Cys Leu Arg Leu Lys Val Thr Val
 145 150 155 160
 Ser Gly Lys Ile Thr His Ser Pro Gln Ala His Asp Asn Pro Gln Glu
 165 170 175
 Lys Arg Leu Ala Ala Asp Asp Pro Glu Val Arg Val Leu His Ser Ile
 180 185 190
 Gly His Ser Ala Ala Pro Arg Leu Phe Pro Leu Ala Trp Thr Val Leu
 195 200 205
 Leu Leu Pro Leu Leu Leu Leu Gln Thr Pro
 210 215

<210> 511

<211> 156

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (156)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 511

Phe Phe Ser His Leu Asp Cys Lys Met Lys Leu Leu Val Leu Ala Val
1 5 10 15

Leu Leu Thr Val Ala Ala Ala Asp Ser Gly Ile Ser Pro Arg Ala Val
20 25 30

Trp Gln Phe Arg Lys Met Ile Lys Cys Val Ile Pro Gly Ser Asp Pro
35 40 45

Phe Leu Glu Tyr Asn Asn Tyr Gly Cys Tyr Cys Gly Leu Gly Gly Ser
50 55 60

Gly Thr Pro Val Asp Glu Leu Asp Lys Cys Cys Gln Thr His Asp Asn
65 70 75 80

Cys Tyr Asp Gln Ala Lys Lys Leu Asp Ser Cys Lys Phe Leu Leu Asp
85 90 95

Asn Pro Tyr Thr His Thr Tyr Ser Tyr Ser Cys Ser Gly Ser Ala Ile
100 105 110

Thr Cys Ser Ser Lys Asn Lys Glu Cys Glu Ala Phe Ile Cys Asn Cys
115 120 125

Asp Arg Asn Ala Ala Ile Cys Phe Ser Lys Ala Pro Tyr Asn Lys Ala
130 135 140

His Lys Asn Leu Asp Thr Lys Lys Tyr Cys Gln Xaa
145 150 155

<210> 512

<211> 169

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (143)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (144)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 512

Glu Ser Arg Pro Ala Asp Arg Arg Val Leu Pro Pro Ile His Val Lys
1 5 10 15

Met Thr Lys Phe Gly Phe Leu Arg Leu Ser Tyr Glu Lys Gln Asp Thr
 20 25 30
 Leu Leu Lys Leu Leu Ile Leu Ser Met Ala Ala Val Leu Ser Phe Ser
 35 40 45
 Thr Arg Leu Phe Ala Val Leu Arg Phe Glu Ser Val Ile His Glu Phe
 50 55 60
 Asp Pro Tyr Phe Asn Tyr Arg Thr Thr Arg Phe Leu Ala Glu Glu Gly
 65 70 75 80
 Phe Tyr Lys Phe His Asn Trp Phe Asp Asp Arg Ala Trp Tyr Pro Leu
 85 90 95
 Gly Arg Ile Ile Gly Gly Thr Ile Tyr Pro Gly Leu Met Ile Thr Ser
 100 105 110
 Ala Ala Ile Tyr His Val Leu His Phe Phe His Ile Thr Ile Asp Ile
 115 120 125
 Arg Asn Val Cys Val Phe Leu Ala Pro Leu Phe Ser Ser Phe Xaa Xaa
 130 135 140
 Ile Val Thr Tyr His Leu Thr Lys Glu Leu Lys Asp Ala Gly Ala Gly
 145 150 155 160
 Leu Leu Ala Ala Ala Met Ile Ala Val
 165

<210> 513

<211> 330

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (10)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 513

Ser Leu Cys Ser Arg Leu Phe Glu Leu Xaa Val Tyr Gln Gln Gly Asp
 1 5 10 15

Leu Asp Lys Ala Leu Leu Leu Thr Lys Lys Leu Leu Glu Leu Asp Pro
 20 25 30

Glu His Gln Arg Ala Asn Gly Asn Leu Lys Tyr Phe Glu Tyr Ile Met

35	40	45
Ala Lys Glu Lys Asp Val Asn Lys Ser Ala Ser Asp Asp Gln Ser Asp		
50	55	60
Gln Lys Thr Thr Pro Lys Lys Lys Gly Val Ala Val Asp Tyr Leu Pro		
65	70	75
Glu Arg Gln Lys Tyr Glu Met Leu Cys Arg Gly Glu Gly Ile Lys Met		
	85	90
Thr Pro Arg Arg Gln Lys Lys Leu Phe Cys Arg Tyr His Asp Gly Asn		
	100	110
Arg Asn Pro Lys Phe Ile Leu Ala Pro Ala Lys Gln Glu Asp Glu Trp		
	115	125
Asp Lys Pro Arg Ile Ile Arg Phe His Asp Ile Ile Ser Asp Ala Glu		
	130	140
Ile Glu Ile Val Lys Asp Leu Ala Lys Pro Arg Leu Arg Arg Ala Thr		
145	150	155
Ile Ser Asn Pro Ile Thr Gly Asp Leu Glu Thr Val His Tyr Arg Ile		
	165	170
Ser Lys Ser Ala Trp Leu Ser Gly Tyr Glu Asn Pro Val Val Ser Arg		
	180	185
Ile Asn Met Arg Ile Gln Asp Leu Thr Gly Leu Asp Val Ser Thr Ala		
	195	200
Glu Glu Leu Gln Val Ala Asn Tyr Gly Val Gly Gly Gln Tyr Glu Pro		
	210	220
His Phe Asp Phe Ala Arg Lys Asp Glu Pro Asp Ala Phe Lys Glu Leu		
225	230	235
Gly Thr Gly Asn Arg Ile Ala Thr Trp Leu Phe Tyr Met Ser Asp Val		
	245	250
Ser Ala Gly Gly Ala Thr Val Phe Pro Glu Val Gly Ala Ser Val Trp		
	260	265
Pro Lys Lys Gly Thr Ala Val Phe Trp Tyr Asn Leu Phe Ala Ser Gly		
	275	280
Glu Gly Asp Tyr Ser Thr Arg His Ala Ala Cys Pro Val Leu Val Gly		
	290	300
Asn Lys Trp Val Ser Asn Lys Trp Leu His Glu Arg Gly Gln Glu Phe		

<220>

<221> SITE

<222> (155)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 515

Ala Glu Asp Val Asp His Asp Gly Gly Leu Gly Gly Leu Gln His His
 1 5 10 15

Pro Thr Pro His Pro Arg Pro Arg Pro Gly Asp Tyr Ser Gln Val Leu
 20 25 30

Phe Glu Arg Pro Gly Ile Trp Lys Asp Leu Lys Thr Met Gly Ser Val
 35 40 45

Ser Leu Ser Ile Phe Phe Ile Thr Leu Leu Val Leu Gly Arg Gln Asn
 50 55 60

Glu Tyr Tyr Cys Arg Leu Asp Phe Leu Trp Lys Asn Lys Phe Lys Lys
 65 70 75 80

Glu Arg Glu Glu Ile Glu Thr Met Glu Asn Leu Asn Arg Val Leu Leu
 85 90 95

Glu Asn Val Leu Pro Ala His Val Ala Glu His Phe Leu Ala Arg Ser
 100 105 110

Leu Lys Asn Glu Glu Leu Tyr His Gln Ser Tyr Asp Cys Val Cys Val
 115 120 125

Met Phe Ala Ser Ile Pro Asp Phe Lys Glu Phe Tyr Thr Glu Ser Asp
 130 135 140

Val Asn Lys Glu Gly Leu Glu Cys Leu Arg Xaa Leu Asn Glu Ile Ile
 145 150 155 160

Ala Asp Phe Asp Asp Leu Leu Ser Lys Pro Lys Phe Ser Gly Val Glu
 165 170 175

Lys Ile Lys Thr Ile Gly Ser Thr Tyr Met Ala Ala Thr Gly Leu Ser
 180 185 190

Ala Val Pro Ser Gln Glu His Ser Gln Glu Pro Glu Arg Gln Tyr Met
 195 200 205

His Ile Gly Thr Met Val Glu Phe Ala Phe Ala Leu Val Gly Lys Leu
 210 215 220

Asp Ala Ile Asn Lys His Ser Phe Asn Asp Phe Lys Leu Arg Val Gly
 225 230 235 240

Ile Asn His Gly Pro Val Ile Ala Gly Val Ile Gly Ala Gln Lys Pro
 245 250 255
 Gln Tyr Asp Ile Trp Gly Asn Thr Val Asn Val Ala Ser Arg Met Asp
 260 265 270
 Ser Thr Gly Val Leu Asp Lys Ile Gln Val Thr Glu Glu Thr Ser Leu
 275 280 285
 Val Leu Gln Thr Leu Gly Tyr Thr Cys Thr Cys Arg Gly Ile Ile Gln
 290 295 300
 Arg Glu Arg Glu Arg Gly Thr
 305 310

<210> 516

<211> 85

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (84)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 516

Ser Gly Leu Leu Val Leu Ser Val Leu Leu Gly Ala Val Phe Gly Lys
 1 5 10 15
 Glu Asp Phe Val Gly His Gln Val Leu Arg Ile Ser Val Ala Asp Glu
 20 25 30
 Ala Gln Val Gln Lys Val Lys Glu Leu Glu Asp Leu Glu His Leu Gln
 35 40 45
 Leu Asp Phe Trp Arg Gly Pro Ala His Pro Gly Ser Pro Ile Asp Val
 50 55 60
 Arg Val Pro Phe Pro Ser Ile Gln Ala Val Lys Ile Phe Leu Glu Phe
 65 70 75 80
 His Gly Ile Xaa Tyr
 85

<210> 517

<211> 406

<212> PRT

<213> Homo sapiens

<400> 517

Gly His Glu Gly Ser Met Arg Gly Leu Leu Val Leu Ser Val Leu Leu
1 5 10 15

Gly Ala Val Phe Gly Lys Glu Asp Phe Val Gly His Gln Val Leu Arg
20 25 30

Ile Ser Val Ala Asp Glu Ala Gln Val Gln Lys Val Lys Glu Leu Glu
35 40 45

Asp Leu Glu His Leu Gln Leu Asp Phe Trp Arg Gly Pro Ala His Pro
50 55 60

Gly Ser Pro Ile Asp Val Arg Val Pro Phe Pro Ser Ile Gln Ala Val
65 70 75 80

Lys Ile Phe Leu Glu Ser His Gly Ile Ser Tyr Glu Thr Met Ile Glu
85 90 95

Asp Val Gln Ser Leu Leu Asp Glu Glu Gln Glu Gln Met Phe Ala Phe
100 105 110

Arg Ser Arg Ala Arg Ser Thr Asp Thr Phe Asn Tyr Ala Thr Tyr His
115 120 125

Thr Leu Glu Glu Ile Tyr Asp Phe Leu Asp Leu Leu Val Ala Glu Asn
130 135 140

Pro His Leu Val Ser Lys Ile Gln Ile Gly Asn Thr Tyr Glu Gly Arg
145 150 155 160

Pro Ile Tyr Val Leu Lys Phe Ser Thr Gly Gly Ser Lys Arg Pro Ala
165 170 175

Ile Trp Ile Asp Thr Gly Ile His Ser Arg Glu Trp Val Thr Gln Ala
180 185 190

Ser Gly Val Trp Phe Ala Lys Lys Ile Thr Gln Asp Tyr Gly Gln Asp
195 200 205

Ala Ala Phe Thr Ala Ile Leu Asp Thr Leu Asp Ile Phe Leu Glu Ile
210 215 220

Val Thr Asn Pro Asp Gly Phe Ala Phe Thr His Ser Thr Asn Arg Met
225 230 235 240

Trp Arg Lys Thr Arg Ser His Thr Ala Gly Ser Leu Cys Ile Gly Val
245 250 255

Asp Pro Asn Arg Asn Trp Asp Ala Gly Phe Gly Leu Ser Gly Ala Ser
260 265 270

Ser Asn Pro Cys Ser Glu Thr Tyr His Gly Lys Phe Ala Asn Ser Glu
275 280 285

Val Glu Val Lys Ser Ile Val Asp Phe Val Lys Asp His Gly Asn Ile
290 295 300

Lys Ala Phe Ile Ser Ile His Ser Tyr Ser Gln Leu Leu Met Tyr Pro
305 310 315 320

Tyr Gly Tyr Lys Thr Glu Pro Val Pro Asp Gln Asp Glu Leu Asp Gln
325 330 335

Leu Ser Lys Ala Ala Val Thr Ala Leu Ala Ser Leu Tyr Gly Thr Lys
340 345 350

Phe Asn Tyr Gly Ser Ile Ile Lys Ala Ile Tyr Gln Ala Ser Gly Ser
355 360 365

Thr Ile Asp Trp Thr Tyr Ser Gln Gly Ile Lys Tyr Ser Phe Thr Phe
370 375 380

Glu Leu Arg Asp Thr Gly Arg Tyr Gly Phe Leu Leu Pro Ala Ser Gln
385 390 395 400

Ile Ile Pro Thr Ala Asn
405

<210> 518

<211> 217

<212> PRT

<213> Homo sapiens

<400> 518

Arg Ala Ala Val Gln Ser Arg His Leu Val Gly Ala Lys Pro Thr Pro
1 5 10 15

Gly Ser Glu Gln Gln Pro Leu Arg Cys Pro Trp Pro Val Ser Phe His
20 25 30

Leu Ser Thr Ser Met Gly Asn Ile Phe Ala Asn Leu Phe Lys Gly Leu
35 40 45

Phe Gly Lys Lys Glu Met Arg Ile Leu Met Val Gly Leu Asp Ala Ala
50 55 60

Gly Lys Thr Thr Ile Leu Tyr Lys Leu Lys Leu Gly Glu Ile Val Thr
 65 70 75 80
 Thr Ile Pro Thr Ile Gly Phe Asn Val Glu Thr Val Glu Tyr Lys Asn
 85 90 95
 Ile Ser Phe Thr Val Trp Asp Val Gly Gly Gln Asp Lys Ile Arg Pro
 100 105 110
 Leu Trp Arg His Tyr Phe Gln Asn Thr Gln Gly Leu Ile Phe Val Val
 115 120 125
 Asp Ser Asn Asp Arg Glu Arg Val Asn Glu Ala Arg Glu Glu Leu Met
 130 135 140
 Arg Met Leu Ala Glu Asp Glu Leu Arg Asp Ala Val Leu Leu Val Phe
 145 150 155 160
 Ala Asn Lys Gln Asp Leu Pro Asn Ala Met Asn Ala Ala Glu Ile Thr
 165 170 175
 Asp Lys Leu Gly Leu His Ser Leu Arg His Arg Asn Trp Tyr Ile Gln
 180 185 190
 Ala Thr Cys Ala Thr Ser Gly Asp Gly Leu Tyr Glu Gly Leu Asp Trp
 195 200 205
 Leu Ser Asn Gln Leu Arg Asn Gln Lys
 210 215

<210> 519

<211> 112

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (86)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (96)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (111)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 519

Leu Leu Phe Leu Lys Arg Cys Ser Val Lys Leu Ala Leu Arg Val Arg
 1 5 10 15

Glu Ala Cys Asp Leu Lys Thr Glu Asn Trp Glu Glu Thr Leu Tyr Pro
 20 25 30

Val Leu Leu Ala Gly Phe Asp Arg Ser Arg Ser Ala Trp Asp Phe Leu
 35 40 45

Lys Leu Cys Pro Lys Leu Gln Leu Trp Glu Trp Arg Asn Lys Gln Ala
 50 55 60

Ser Pro Arg Ile Val Lys Glu Ile Ala Leu Val Asp Glu Thr Lys Thr
 65 70 75 80

Asn Ala Leu Asp Phe Xaa Ala Leu Pro Gly Val Val Thr Arg Gly Xaa
 85 90 95

Asn Val Cys Gly His Ile Leu Asn Ser Lys Val Phe Ser Ser Xaa Gly
 100 105 110

<210> 520

<211> 71

<212> PRT

<213> Homo sapiens

<400> 520

Lys Ala Arg Val Gln Ile Arg Leu Val Ser Leu Val Gly Asp Tyr Phe
 1 5 10 15

Trp Val His Ser Val Val Gln Glu Thr Leu Val Lys His Leu Leu Leu
 20 25 30

Leu Asp Thr Met Leu Asp Thr Glu Asp Asn Glu Gly Lys Ile Asp Ile
 35 40 45

Val Pro Ala Leu Met Glu Leu Ile Val Ser Cys Gly Leu Ser Glu Gln
 50 55 60

Ser Leu Asn Leu Leu Leu Tyr
 65 70

<210> 521
<211> 183
<212> PRT
<213> Homo sapiens

<400> 521
Ala Ala Val Asn His Leu Gln Ser Ala Gly Ser Thr Ser Pro Ile Leu
1 5 10 15
Ala Ala Ala Gln Ser Leu His Arg Glu Ala Thr Lys Trp Ser Ser Lys
20 25 30
Gly Asn Asp Ile Ile Ala Ala Ala Lys Arg Met Ala Leu Leu Met Ala
35 40 45
Glu Met Ser Arg Leu Val Arg Gly Gly Ser Gly Thr Lys Arg Ala Leu
50 55 60
Ile Gln Cys Ala Lys Asp Ile Ala Lys Ala Ser Asp Glu Val Thr Arg
65 70 75 80
Leu Ala Lys Glu Val Ala Lys Gln Cys Thr Asp Lys Arg Ile Arg Thr
85 90 95
Asn Leu Leu Gln Val Cys Glu Arg Ile Pro Thr Ile Ser Thr Gln Leu
100 105 110
Lys Ile Leu Ser Thr Val Lys Ala Thr Met Leu Gly Arg Thr Asn Ile
115 120 125
Ser Asp Glu Glu Ser Glu Gln Ala Thr Glu Met Leu Val His Asn Ala
130 135 140
Gln Asn Leu Met Gln Ser Val Lys Glu Thr Val Arg Glu Ala Glu Ala
145 150 155 160
Ala Ser Ile Lys Ile Arg Thr Asp Ala Gly Phe Thr Leu Arg Trp Val
165 170 175
Arg Lys Thr Pro Trp Tyr Gln
180

<210> 522
<211> 80
<212> PRT
<213> Homo sapiens

<400> 522
Asn His Leu Thr Ile Lys Trp Thr Thr Glu Asn Ser Pro Ser Cys Leu

462

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      1             5             10             15
Lys Ala Ser Pro Thr Val Val Ile Leu Gln Ala Ala Thr Cys Asn Leu
      20             25             30
Asp Val Val Ser Thr Cys Ser Ala Gly Tyr Asp Ser Cys Ile Leu Gly
      35             40             45
Leu Ala Phe Phe Cys Val Ile Asn Tyr Gly Tyr Pro Leu Asn Arg His
      50             55             60
Leu Met Lys His Cys Thr Asn Cys His Ser Phe Asp Asp Thr Trp Glu
      65             70             75             80

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<210> 523
 <211> 41
 <212> PRT
 <213> Homo sapiens

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<400> 523
Pro Asn Gln Trp Leu Cys Ser Thr Gln Cys Pro Ser Gly Glu Thr Glu
  1             5             10             15
Gly Gln Arg Gly Glu Gly Thr Cys Pro Arg Ser His Gly Asp Gly Thr
      20             25             30
Pro Arg Ala Gly Pro Leu Val Arg Ala
      35             40

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<210> 524
 <211> 374
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (76)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (77)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (78)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 524

Glu Gly Gln Ser Ser Ala Leu Ala Gly Gln Gly Ala Ala Gln Arg Ala
1 5 10 15

Gly Asp Pro Gly Ala Ala Arg Ala Arg Pro Arg Leu Arg Ser Gly Ser
20 25 30

Gln Arg Gln Pro Gly Ala His Gly Pro Ser Ala His Gly Ser Thr Met
35 40 45

Pro Ala Leu Leu Glu Arg Pro Lys Leu Ser Asn Ala Met Ala Arg Ala
50 55 60

Leu His Arg His Ile Met Met Glu Arg Glu Arg Xaa Xaa Xaa Glu Glu
65 70 75 80

Glu Glu Val Asp Lys Met Met Glu Gln Lys Met Lys Glu Glu Gln Glu
85 90 95

Arg Arg Lys Lys Lys Glu Met Glu Glu Arg Met Ser Leu Glu Glu Thr
100 105 110

Lys Glu Gln Ile Leu Lys Leu Glu Glu Lys Leu Leu Ala Leu Gln Glu
115 120 125

Glu Lys His Gln Leu Phe Leu Gln Leu Lys Lys Val Leu His Glu Glu
130 135 140

Glu Lys Arg Arg Arg Lys Glu Gln Ser Asp Leu Thr Thr Leu Thr Ser
145 150 155 160

Ala Ala Tyr Gln Gln Ser Leu Thr Val His Thr Gly Thr His Leu Leu
165 170 175

Ser	Met	Gln	Gly	Ser	Pro	Gly	Gly	His	Asn	Arg	Pro	Gly	Thr	Leu	Met
			180					185					190		

Ala Ala Asp Arg Ala Lys Gln Met Phe Gly Pro Gln Val Leu Thr Thr
195 200 205

Arg His Tyr Val Gly Ser Ala Ala Ala Phe Ala Gly Thr Pro Glu His
210 215 220

Gly Gln Phe Gln Gly Ser Pro Gly Gly Ala Tyr Gly Thr Ala Gln Pro
225 230 235 240

Pro Pro His Tyr Gly Pro Thr Gln Pro Ala Tyr Ser Pro Ser Gln Gln
 245 250 255
 Leu Arg Ala Pro Ser Ala Phe Pro Ala Val Gln Tyr Leu Ser Gln Pro
 260 265 270
 Gln Pro Gln Pro Tyr Ala Val His Gly His Phe Gln Pro Thr Gln Thr
 275 280 285
 Gly Phe Leu Gln Pro Gly Gly Ala Leu Ser Leu Gln Lys Gln Met Glu
 290 295 300
 His Ala Asn Gln Gln Thr Gly Phe Ser Asp Ser Ser Ser Leu Arg Pro
 305 310 315 320
 Met His Pro Gln Ala Leu His Pro Ala Pro Gly Leu Leu Ala Ser Pro
 325 330 335
 Gln Leu Pro Val Gln Met Gln Pro Ala Gly Lys Ser Gly Phe Ala Ala
 340 345 350
 Thr Ser Gln Pro Gly Pro Arg Leu Pro Phe Ile Gln His Ser Gln Asn
 355 360 365
 Pro Arg Phe Tyr His Lys
 370

<210> 525
 <211> 100
 <212> PRT
 <213> Homo sapiens

<400> 525
 Gly Ser His Cys Tyr Tyr Phe Asn Glu Glu His Glu Thr Trp Val Tyr
 1 5 10 15
 Ala Asp Leu Tyr Cys Gln Asn Met Asn Ser Gly Asn Leu Val Ser Val
 20 25 30
 Leu Thr Gln Ala Glu Gly Ala Phe Val Ala Ser Leu Ile Lys Glu Ser
 35 40 45
 Gly Thr Lys Asp Ser Asn Val Trp Ile Gly Leu His Asp Pro His Arg
 50 55 60
 Ile Ser Leu Leu His Leu Leu Pro Pro Asp Tyr Gln Val Pro Glu Gly
 65 70 75 80
 Leu Met Ser Gly Thr Ser Ser Ile Ser Phe Tyr Tyr Ile Met Ile Lys

85 90 95

Ala Thr Ser Leu
100

<210> 526
<211> 104
<212> PRT
<213> Homo sapiens

<400> 526
Arg Leu His Thr Met Asp Ser Phe Ser Gln Asp Val Lys Thr Arg Leu
1 5 10 15
Leu Ile Met Ile Arg Leu Leu Pro Pro Phe Asn Leu Ser Leu Leu Met
20 25 30
Pro Ala Ser Phe Ala Trp Gln Asp Asp Ala Val Ile Ser Ile Ser Gln
35 40 45
Glu Val Ala Ser Glu Gly Asn Leu Thr Glu Tyr Gln Ile Tyr Leu Val
50 55 60
Asn Pro Asn Val Leu His Lys Ile Arg Asp Pro Leu Val His Pro Val
65 70 75 80
Thr Asp Ile Ser Ser Ile Phe Asn Thr Ala Val Cys Ser Asn Val Gln
85 90 95
Trp Ser Phe Ser Glu Leu Asp Phe
100

<210> 527
<211> 123
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (64)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (81)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (99)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (106)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (108)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 527
 Phe Pro Ser Ile Ser Arg Ala Val Asp Asp Glu Ile Glu Ala Asn Leu
 1 5 10 15
 Glu Glu Phe Asp Ile Ser Glu Asp Asp Ile Asp Asp Gly Phe Arg Arg
 20 25 30
 Leu Phe Ala Gln Leu Ala Gly Glu Asp Ala Glu Ile Ser Ala Phe Xaa
 35 40 45
 Leu Gln Thr Ile Leu Arg Arg Val Leu Ala Lys Arg Gln Asp Ile Xaa
 50 55 60
 Ser Asp Gly Phe Ser Ile Glu Thr Cys Lys Ile Met Val Asp Met Leu
 65 70 75 80
 Xaa Ser Asp Gly Ser Gly Lys Leu Gly Leu Lys Glu Phe Tyr Ile Leu
 85 90 95
 Trp Thr Xaa Ile Gln Lys Tyr Gln Val Xaa Ser Xaa Lys Cys Gly Trp
 100 105 110
 Ile Cys Val Gly Lys His Ser Val His Met Leu
 115 120

<210> 528
 <211> 428
 <212> PRT
 <213> Homo sapiens

<220>

<221> SITE

<222> (7)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (117)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (124)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (258)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 528

Gly	Arg	Met	Gly	Thr	Pro	Xaa	Lys	Pro	Met	Ala	Met	Arg	Leu	Ile	Leu
1				5				10					15		

Phe	Phe	Gly	Ala	Leu	Phe	Gly	His	Ile	Tyr	Cys	Leu	Glu	Thr	Phe	Val
		20					25						30		

Gly	Asp	Gln	Val	Leu	Glu	Ile	Val	Pro	Ser	Asn	Glu	Glu	Gln	Ile	Lys
	35					40						45			

Asn	Leu	Leu	Gln	Leu	Glu	Ala	Gln	Glu	His	Leu	Gln	Leu	Asp	Phe	Trp
	50					55						60			

Lys	Ser	Pro	Thr	Thr	Pro	Gly	Glu	Thr	Ala	His	Val	Arg	Val	Pro	Phe
65					70					75				80	

Val	Asn	Val	Gln	Ala	Val	Lys	Val	Phe	Leu	Glu	Ser	Gln	Gly	Ile	Ala
		85						90						95	

Tyr	Ser	Ile	Met	Ile	Glu	Asp	Val	Gln	Val	Leu	Leu	Asp	Lys	Glu	Asn
		100						105					110		

Glu	Glu	Met	Leu	Xaa	Asn	Arg	Arg	Arg	Glu	Arg	Xaa	Val	Asn	Phe	Asn
		115					120					125			

Phe	Gly	Ala	Tyr	His	Thr	Leu	Glu	Glu	Ile	Ser	Gln	Glu	Met	Asp	Asn
	130					135						140			

Leu	Val	Ala	Glu	His	Pro	Gly	Leu	Val	Ser	Lys	Val	Asn	Ile	Gly	Ser
145						150				155				160	

Ser Phe Glu Asn Arg Pro Met Asn Val Leu Lys Phe Ser Thr Gly Gly
 165 170 175
 Asp Lys Pro Ala Ile Trp Leu Asp Ala Gly Ile His Ala Arg Glu Trp
 180 185 190
 Val Thr Gln Ala Thr Ala Leu Trp Thr Ala Asn Lys Ile Val Ser Asp
 195 200 205
 Tyr Gly Lys Asp Pro Ser Ile Thr Ser Ile Leu Asp Ala Leu Asp Ile
 210 215 220
 Phe Leu Leu Pro Val Thr Asn Pro Asp Gly Tyr Val Phe Ser Gln Thr
 225 230 235 240
 Lys Asn Arg Met Trp Arg Lys Thr Arg Ser Lys Val Ser Gly Ser Leu
 245 250 255
 Cys Xaa Gly Val Asp Pro Asn Arg Asn Trp Asp Ala Gly Phe Gly Gly
 260 265 270
 Pro Gly Ala Ser Ser Asn Pro Cys Ser Asp Ser Tyr His Gly Pro Ser
 275 280 285
 Ala Asn Ser Glu Val Glu Val Lys Ser Ile Val Asp Phe Ile Lys Ser
 290 295 300
 His Gly Lys Val Lys Ala Phe Ile Thr Leu His Ser Tyr Ser Gln Leu
 305 310 315 320
 Leu Met Phe Pro Tyr Gly Tyr Lys Cys Thr Lys Leu Asp Asp Phe Asp
 325 330 335
 Glu Leu Ser Glu Val Ala Gln Lys Ala Ala Gln Ser Leu Arg Ser Leu
 340 345 350
 His Gly Thr Lys Tyr Lys Val Gly Pro Ile Cys Ser Val Ile Tyr Gln
 355 360 365
 Ala Ser Gly Gly Ser Ile Asp Trp Ser Tyr Asp Tyr Gly Ile Lys Tyr
 370 375 380
 Ser Phe Ala Phe Glu Leu Arg Asp Thr Gly Arg Tyr Gly Phe Leu Leu
 385 390 395 400
 Pro Ala Arg Gln Ile Leu Pro Thr Ala Glu Glu Thr Trp Leu Gly Leu
 405 410 415
 Lys Ala Ile Met Glu His Val Arg Asp His Pro Tyr
 420 425

<210> 529

<211> 192

<212> PRT

<213> Homo sapiens

<400> 529

Ser Leu Thr Leu Ser Leu Val Leu Leu Gly Ser Ser Trp Gly Cys Gly
1 5 10 15

Ile Pro Ala Ile Lys Pro Ala Leu Ser Phe Ser Gln Arg Ile Val Asn
20 25 30

Gly Glu Asn Ala Val Leu Gly Ser Trp Pro Trp Gln Val Ser Leu Gln
35 40 45

Asp Ser Ser Gly Phe His Phe Cys Gly Gly Ser Leu Ile Ser Gln Ser
50 55 60

Trp Val Val Thr Ala Ala His Cys Asn Val Ser Pro Gly Arg His Phe
65 70 75 80

Val Val Leu Gly Glu Tyr Asp Arg Ser Ser Asn Ala Glu Pro Leu Gln
85 90 95

Val Leu Ser Val Ser Arg Ala Ile Thr His Pro Ser Trp Asn Ser Thr
100 105 110

Thr Met Asn Asn Asp Val Thr Leu Leu Lys Leu Ala Ser Pro Ala Gln
115 120 125

Tyr Thr Thr Arg Ile Ser Pro Val Cys Leu Ala Ser Ser Asn Glu Ala
130 135 140

Leu Thr Glu Gly Leu Thr Cys Val Thr Thr Gly Trp Gly Arg Leu Ser
145 150 155 160

Gly Val Gly Asn Val Thr Pro Ala His Leu Gln Gln Val Ala Leu Pro
165 170 175

Leu Val Thr Val Asn Gln Cys Arg Gln Tyr Trp Gly Ser Ser Tyr His
180 185 190

<210> 530

<211> 321

<212> PRT

<213> Homo sapiens

<400> 530

Gly Gln Ser Thr Ala Ser Pro Ala Phe Ser Ala Ala Pro Gln Pro Arg
 1 5 10 15
 Ala Leu Ser Phe Pro Ala Leu Pro Cys Leu Ala Phe Gln Cys Ser Ser
 20 25 30
 Phe Cys Glu Met Thr Leu Lys Ala Ser Glu Gly Glu Ser Gly Gly Ser
 35 40 45
 Met His Thr Ala Leu Ser Asp Leu Tyr Leu Glu His Leu Leu Gln Lys
 50 55 60
 Arg Ser Arg Pro Glu Ala Val Ser His Pro Leu Asn Thr Val Thr Glu
 65 70 75 80
 Asp Met Tyr Thr Asn Gly Ser Pro Ala Pro Gly Ser Pro Ala Gln Val
 85 90 95
 Lys Gly Gln Glu Val Arg Lys Val Arg Leu Ile Gln Phe Glu Lys Val
 100 105 110
 Thr Glu Glu Pro Met Gly Ile Thr Leu Lys Leu Asn Glu Lys Gln Ser
 115 120 125
 Cys Thr Val Ala Arg Ile Leu His Gly Gly Met Ile His Arg Gln Gly
 130 135 140
 Ser Leu His Val Gly Asp Glu Ile Leu Glu Ile Asn Gly Thr Asn Val
 145 150 155 160
 Thr Asn His Ser Val Asp Gln Leu Gln Lys Ala Met Lys Glu Thr Lys
 165 170 175
 Gly Met Ile Ser Leu Lys Val Ile Pro Asn Gln Gln Ser Arg Leu Pro
 180 185 190
 Ala Leu Gln Met Phe Met Arg Ala Gln Phe Asp Tyr Asp Pro Lys Lys
 195 200 205
 Asp Asn Leu Ile Pro Cys Lys Glu Ala Gly Leu Lys Phe Ala Thr Gly
 210 215 220
 Asp Ile Ile Gln Ile Ile Asn Lys Asp Asp Ser Asn Trp Trp Gln Gly
 225 230 235 240
 Arg Val Glu Gly Ser Ser Lys Glu Ser Ala Gly Leu Ile Pro Ser Pro

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                245                250                255
Glu Leu Gln Glu Trp Arg Val Ala Ser Met Ala Gln Ser Ala Pro Ser
                260                265                270
Glu Ala Arg Ala Ala Val Pro Leu Gly Arg Arg Arg Ser Thr Lys Thr
                275                280                285
Asn Ile Trp Pro Ser Thr Ala Arg Phe Leu Ile Ser Trp Met Leu Phe
                290                295                300
Pro Thr Arg Lys Ser Phe Gly Ser Leu His Ser Arg Gly Arg Pro Trp
                305                310                315                320

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Cys

<210> 531
 <211> 390
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (3)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (84)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 531
 Gln Arg Xaa Ser Gly Thr Phe Thr Met Gly Arg Lys Ser Leu Tyr Leu
 1 5 10 15

Leu Ile Val Gly Ile Leu Ile Ala Tyr Tyr Ile Tyr Thr Pro Leu Pro
 20 25 30

Asp Asn Val Glu Glu Pro Trp Arg Met Met Trp Ile Asn Ala His Leu
 35 40 45

Lys Thr Ile Gln Asn Leu Val Val Gly Ser Phe Asp Glu Val Pro Pro
 50 55 60

Thr Ser Asp Glu Asn Val Thr Val Thr Glu Thr Lys Phe Asn Asn Ile
 65 70 75 80

Leu Val Arg Xaa Tyr Val Pro Lys Arg Lys Ser Glu Ala Leu Arg Arg

Gln Val Thr His Asn His Val Glu Asp Gly Phe His Gly Ala Phe Ser

473

355 360 365
 Phe Leu Gly Leu Lys Ile Ser His Arg Leu Ile Asn Gln Tyr Ile Glu
 370 375 380
 Trp Leu Lys Glu Asn Leu
 385 390

<210> 532
 <211> 261
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (8)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (242)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (245)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (256)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (260)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 532
 Gly Val Gly Tyr Asn Thr Val Xaa Ser Pro Pro Ala Pro Ser Phe Cys
 1 5 10 15

Asn Met Gly Lys Asn Lys Leu Leu His Pro Ser Leu Val Leu Leu Leu
 20 25 30

Leu Val Leu Leu Pro Thr Asp Ala Ser Val Ser Gly Lys Pro Gln Tyr
 35 40 45

Met Val Leu Val Pro Ser Leu Leu His Thr Glu Thr Thr Glu Lys Gly

474

50	55	60
Cys Val Leu Leu Ser Tyr Leu Asn Glu Thr Val Thr Val Ser Ala Ser		
65	70	75 80
Leu Glu Ser Val Arg Gly Asn Arg Ser Leu Phe Thr Asp Leu Glu Ala		
85	90	95
Glu Asn Asp Val Leu His Cys Val Ala Phe Ala Val Pro Lys Ser Ser		
100	105	110
Ser Asn Glu Glu Val Met Phe Leu Thr Val Gln Val Lys Gly Pro Thr		
115	120	125
Gln Glu Phe Lys Lys Arg Thr Thr Val Met Val Lys Asn Glu Asp Ser		
130	135	140
Leu Val Phe Val Gln Thr Asp Lys Ser Ile Tyr Lys Pro Gly Gln Thr		
145	150	155 160
Val Lys Phe Arg Val Val Ser Met Asp Glu Asn Phe His Pro Leu Asn		
165	170	175
Glu Leu Ile Pro Leu Val Tyr Ile Gln Asp Pro Lys Gly Asn Arg Ile		
180	185	190
Ala Gln Trp Gln Ser Phe Gln Leu Glu Gly Gly Leu Lys Gln Phe Ser		
195	200	205
Phe Pro Leu Ser Ser Glu Pro Phe Gln Gly Ser Leu Gln Gly Gly Gly		
210	215	220
Thr Glu Glu Ile Arg Trp Glu Gly Thr Glu His Pro Phe His Arg Gly		
225	230	235 240
Arg Xaa Cys Cys Xaa Pro Lys Phe Gly Ser Tyr Lys Leu Thr Val Xaa		
245	250	255
Lys Gly Asn Xaa His		
260		

<210> 533

<211> 73

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (24)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (32)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 533

Asn Arg Ser Val Gln Ser Tyr Phe Phe Leu Thr Leu Asn Phe Pro Ser
1 5 10 15

Arg Glu Tyr Thr Ile Trp Leu Xaa Gly Arg Gly Ser Pro Glu Glu Xaa
20 25 30

Gly Phe Ala Leu Arg Gly Arg Ala Ser Leu Asp Phe Ala Ala Ser Asn
35 40 45

Phe Ser Arg Gly Val Glu Gly Gly Ala Leu Gly Gly Pro His Ser Leu
50 55 60

Ser Gly Val Pro Ala Arg Val Ser Phe
65 70

<210> 534

<211> 150

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (1)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 534

Xaa Arg Lys Gln Gln Arg Arg Leu Tyr Pro Val Ser Pro Pro Pro Ser
1 5 10 15

Leu Leu Arg Leu Pro Ser Arg Ala Pro Tyr Thr Pro Gln Ser Arg Ser
20 25 30

Arg His Val Pro Glu Thr Arg Arg Arg Glu Pro Cys Gly Gly Asp Arg
35 40 45

Arg Gly Glu Ala Gly His Ala Glu Lys Glu Gly Ile Leu Pro Glu Arg
50 55 60

Ala Glu Glu Ala Lys Leu Lys Ala Lys Tyr Pro Ser Leu Gly Gln Lys
65 70 75 80

Pro Gly Gly Ser Asp Phe Leu Met Lys Arg Leu Gln Lys Gly Gln Lys
85 90 95

Tyr Phe Asp Ser Gly Asp Tyr Asn Met Ala Lys Ala Lys Met Lys Asn
100 105 110

Lys Gln Leu Pro Ser Ala Gly Pro Asp Lys Asn Leu Val Thr Gly Asp
115 120 125

His Ile Pro Thr Pro Gln Asp Leu Pro Gln Arg Lys Ser Ser Leu Val
130 135 140

Thr Ser Lys Leu Ala Gly
145 150

<210> 535

<211> 67

<212> PRT

<213> Homo sapiens

<400> 535

Gln Ile Val Lys Ile Glu Ala Ile Ala Gln His Arg Phe Ser Ile Asn
1 5 10 15

Ala Val Asn Leu Pro Tyr Leu Arg Lys Asn Ser Leu Thr Leu Glu Tyr
20 25 30

Cys Ile Glu Leu Ser Tyr Thr His Lys Thr Phe Ser Leu Val Asn Gln
35 40 45

Asp Pro Val Arg Val Ser Leu Glu Leu Phe Trp Asn Asn Ala Arg Ile
50 55 60

Gln Thr Asp
65

<210> 536

<211> 107

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (57)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (80)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (85)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (103)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 536

His	Ala	Ser	Gly	Arg	Pro	Pro	Arg	Cys	Trp	Arg	Pro	Ala	Trp	Arg	Gly
1					5				10					15	

Cys	Ser	Ser	Thr	Arg	Arg	Cys	Ser	Thr	Pro	Cys	Ser	Ala	Gly	Arg	Cys
			20					25					30		

Arg	Val	Gly	Arg	Thr	Gly	Thr	Gly	Thr	Thr	Ala	Ser	Thr	Pro	Pro	Cys
		35				40						45			

Cys	Trp	Ala	Arg	Cys	Arg	Cys	Gly	Xaa	Asp	Ala	Pro	Leu	Val	Gln	Asp
	50					55					60				

Glu	Asn	Val	Arg	Gly	Val	Ile	Thr	Met	Asn	Glu	Glu	Tyr	Glu	Thr	Xaa
65					70					75					80

Phe	Leu	Cys	Asn	Xaa	Ser	Gln	Val	His	Lys	Trp	Asn	Pro	Glu	Glu	Ala
			85						90					95	

Val	Arg	Pro	Ser	Pro	Arg	Xaa	Gly	His	Thr	Ser
		100					105			

<210> 537

<211> 49

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (39)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 537

Asn	Gln	Ile	Asn	Phe	Cys	Leu	Asn	Gly	Lys	Tyr	Thr	Tyr	Ile	Cys	Ile
1				5					10					15	

Asp Thr Leu Pro Leu Tyr Met Phe Asn Ile His Thr Leu Lys His Ile
 20 25 30

Asn Thr Ser Val Ile Ile Xaa Trp Ser Leu Gln Tyr Ser Ile Lys Asp
 35 40 45

Lys

<210> 538
 <211> 149
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (62)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (122)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (145)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 538
 Ala Gln Ala Arg Val Pro Ala Thr Thr Ala Ser Pro Gly Gly Pro Ala
 1 5 10 15

Ile Phe Pro Pro Gln Thr Ser Pro Gln Gly Pro Glu Trp Lys Arg Pro
 20 25 30

Ser Asp Pro Pro Phe Gln Pro Ser Pro Pro Ser Gln Lys Leu Thr Gly
 35 40 45

Pro Ala Pro Thr Ser Ser Thr Ala Gly His Pro Pro Pro Xaa Ala Pro
 50 55 60

Leu Pro Thr Pro Arg Gly Thr Arg Arg Thr Ala Cys Pro Pro Ser Ala
 65 70 75 80

Leu Pro Ala Ala Pro Thr Pro Pro Ser Leu Ser Ala Pro Cys Thr Gln
 85 90 95

Ser Pro Ala Cys Leu Cys Ala Pro His Ser His Cys Pro Arg Arg Arg
 100 105 110

Arg Ser Arg Ser His Trp Cys Leu Arg Xaa Ala Leu Gly Glu Ala Val
 115 120 125

Leu Ser Ala Leu Leu Gln Arg Leu Gln Arg Pro Arg Asp His His Val
 130 135 140

Xaa Ala His Val Leu
 145

<210> 539

<211> 61

<212> PRT

<213> Homo sapiens

<400> 539

Glu Met Tyr Val Leu Leu Leu Leu Ile Lys Gly Ile Val Glu Tyr Lys
 1 5 10 15

Arg Phe Phe Lys Leu Val Leu Ser Leu Ile Gly Phe Tyr Asn Pro His
 20 25 30

Phe Lys Glu Glu Met His Leu Thr Phe Asn Asn Leu Val Lys Lys Tyr
 35 40 45

Asn Val Ala Leu Pro Cys Ile Thr Phe Asn Tyr Cys Lys
 50 55 60

<210> 540

<211> 148

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (112)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 540

Gly Gly Gly Ala Gly Leu Gln Gly Leu Pro Gly Ala Arg Gly Gly Leu
 1 5 10 15

Gly Pro Gly Ser Arg Ala Ala Ser Ser Leu Leu Gly Arg Ala Ala Thr
 20 25 30

480

Gly Glu Val Leu Gly Ala Gly Gly Ser Pro Arg Ala Gly Val Thr Pro
35 40 45

Thr Phe Thr Ala Pro Lys Asn Thr Ser Arg Val Gly Gly Gly Gly His
50 55 60

Arg Ala Thr Ser Arg Ser Gly Phe Cys Pro Ser Ser Leu Phe Thr Arg
65 70 75 80

Arg Asn Phe Arg Pro Asp Val Phe Ser Gln Asn Arg Asn Thr Ser Gln
85 90 95

Gly Gln Thr Asp Arg Lys Arg Gly Cys Leu Ala Val Ala Pro His Xaa
100 105 110

Pro Thr Gly Phe Arg Ala Pro Glu Leu Ala Ala Ala Pro Ser Leu Glu
115 120 125

Gln Ser Phe Met Gln Arg Gly Cys Phe Leu Lys Leu Ser Val His Gly
130 135 140

Asp Phe Phe Phe
145

<210> 541

<211> 30

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (12)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 541

Phe Tyr Phe Thr Ser Ile Leu Gln Val Glu Leu Xaa Gly Arg Val Val
1 5 10 15

Ser Asn Pro Lys Leu Val Ile Pro Val Pro Arg Gly His His
20 25 30

<210> 542

<211> 241

<212> PRT

<213> Homo sapiens

<400> 542

Glu Leu Leu Ala Leu Asp Gln Leu His Gly Ser Arg Arg Gln Leu Gln
 1 5 10 15
 Trp Leu Val Gly Glu Leu Gln Ala Ala Glu Asp Arg Gly Asp Lys Val
 20 25 30
 His Ile Ile Gly His Ile Pro Pro Gly His Cys Leu Lys Ser Trp Ser
 35 40 45
 Trp Asn Tyr Tyr Arg Ile Val Ala Arg Tyr Glu Asn Thr Leu Ala Ala
 50 55 60
 Gln Phe Phe Gly His Thr His Val Asp Glu Phe Glu Val Phe Tyr Asp
 65 70 75 80
 Glu Glu Thr Leu Ser Arg Pro Leu Ala Val Ala Phe Leu Ala Pro Ser
 85 90 95
 Ala Thr Thr Tyr Ile Gly Leu Asn Pro Gly Tyr Arg Val Tyr Gln Ile
 100 105 110
 Asp Gly Asn Tyr Ser Gly Ser Ser His Val Val Leu Asp His Glu Thr
 115 120 125
 Tyr Ile Leu Asn Leu Thr Gln Ala Asn Ile Pro Gly Ala Ile Pro His
 130 135 140
 Trp Gln Leu Leu Tyr Arg Ala Arg Glu Thr Tyr Gly Leu Pro Asn Thr
 145 150 155 160
 Leu Pro Thr Ala Trp His Asn Leu Val Tyr Arg Met Arg Gly Asp Met
 165 170 175
 Gln Leu Phe Gln Thr Phe Trp Phe Leu Tyr His Lys Gly His Pro Pro
 180 185 190
 Ser Glu Pro Cys Gly Thr Pro Cys Arg Leu Ala Thr Leu Cys Ala Gln
 195 200 205
 Leu Ser Ala Arg Ala Asp Ser Pro Ala Leu Cys Arg His Leu Met Pro
 210 215 220
 Asp Gly Ser Leu Pro Glu Ala Gln Ser Leu Trp Pro Arg Pro Leu Phe
 225 230 235 240
 Cys

<210> 543

<211> 89

<212> PRT

<213> Homo sapiens

<400> 543

Arg Asn Arg Lys Asn Thr Asp Gly His Gln Gln Phe Phe Ala Ile Val
1 5 10 15

Gln Leu Ile Gly Thr Arg Lys Gln Ala Glu Asn Phe Ala Tyr Arg Leu
20 25 30

Glu Leu Asn Gly His Arg Arg Arg Leu Thr Trp Glu Ala Thr Pro Arg
35 40 45

Ser Ile His Glu Gly Ile Ala Thr Ala Ile Met Asn Ser Asp Cys Leu
50 55 60

Val Phe Asp Thr Ser Ile Ala Gln Leu Phe Ala Glu Asn Gly Asn Leu
65 70 75 80

Gly Ile Asn Val Thr Ile Ser Met Cys
85

<210> 544

<211> 74

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (65)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 544

Gly Ile Gln Ala Ala Pro Gly Arg Gly Arg Leu Arg Leu Tyr Pro Gly
1 5 10 15

Pro Arg Ser Pro Arg Asp Arg Gln Met Arg Ala Ala Gly Pro Gly His
20 25 30

Met Ser Ser Ala Thr Asp Ala Thr Xaa Pro Ala Leu Asp Met Pro Asp
35 40 45

Arg Val Ser Thr Arg Pro Trp Asp Trp Ser Pro Asp Ser Ala Cys Pro

Met Glu Gln Asp Ala Ser Ser Ser Pro Ser Ala Gln Val Ile Gly Leu
 210 215 220

Lys Asn Ala Leu Ser Ser Ala Leu Ala Gln Asn Thr Asp Leu Lys Glu
 225 230 235 240

Arg Leu Arg Arg Ile His Ala Glu Ser Leu Leu Leu Asp Ser Pro Ala
 245 250 255

Val Ala Lys Ser Gly Asp Asn Leu Gly Arg Gly Lys Leu Gln Arg
 260 265 270

<210> 546

<211> 301

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (215)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (292)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 546

Asp Pro Arg Val Arg Glu Asn Ala Arg Leu Phe His Pro Lys Leu Ile
 1 5 10 15

Ile Ala Gly Thr Ser Cys Tyr Ser Arg Asn Leu Glu Tyr Ala Arg Leu
 20 25 30

Arg Lys Ile Ala Asp Glu Asn Gly Ala Tyr Leu Met Ala Asp Met Ala
 35 40 45

His Ile Ser Gly Leu Val Ala Ala Gly Val Val Pro Ser Pro Phe Glu
 50 55 60

His Cys His Val Val Thr Thr Thr Thr His Lys Thr Leu Arg Gly Cys
 65 70 75 80

Arg Ala Gly Met Ile Phe Tyr Arg Lys Gly Val Lys Ser Val Asp Pro
 85 90 95

Lys Thr Gly Lys Glu Ile Leu Tyr Asn Leu Glu Ser Leu Ile Asn Ser
 100 105 110

Ala Val Phe Pro Gly Leu Gln Gly Gly Pro His Asn His Ala Ile Ala
115 120 125

Gly Val Ala Val Ala Leu Lys Gln Ala Met Thr Leu Glu Phe Lys Val
130 135 140

Tyr Gln His Gln Val Val Ala Asn Cys Arg Ala Leu Ser Glu Ala Leu
145 150 155 160

Thr Glu Leu Gly Tyr Lys Ile Val Thr Gly Gly Ser Asp Asn His Leu
165 170 175

Ile Leu Val Asp Leu Arg Ser Lys Gly Thr Asp Gly Gly Arg Ala Glu
180 185 190

Lys Val Leu Glu Ala Cys Ser Ile Ala Cys Asn Lys Asn Thr Cys Pro
195 200 205

Gly Asp Arg Ser Ala Leu Xaa Pro Ser Gly Leu Arg Leu Gly Thr Pro
210 215 220

Ala Leu Thr Ser Arg Gly Leu Leu Glu Lys Asp Phe Gln Lys Val Ala
225 230 235 240

His Phe Ile His Arg Gly Ile Glu Leu Thr Leu Gln Ile Gln Ser Asp
245 250 255

Thr Gly Val Arg Ala Thr Leu Lys Glu Phe Lys Glu Arg Leu Ala Gly
260 265 270

Asp Lys Tyr Gln Ala Ala Val Gln Ala Leu Arg Glu Glu Val Glu Ser
275 280 285

Phe Ala Ser Xaa Phe Pro Leu Pro Gly Leu Pro Asp Phe
290 295 300

<210> 547

<211> 61

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (42)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (47)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (48)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (55)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 547

Glu	Thr	Ser	Arg	Thr	Ser	Gly	Ser	Cys	Ser	Trp	Arg	Ala	Gly	Ala	Pro
1				5					10					15	

Ala	Pro	Leu	Leu	Pro	Thr	His	His	Ile	Leu	Pro	Ile	Leu	Leu	Gln	Gly
		20						25				30			

Pro	Arg	Leu	Leu	Ser	Asn	Ser	Trp	Asp	Xaa	Arg	Pro	Trp	Arg	Xaa	Xaa
		35					40					45			

Pro	Leu	Leu	Gly	Ser	Ala	Xaa	Arg	Pro	Pro	Thr	Leu	Leu
	50					55					60	

<210> 548

<211> 92

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (8)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (9)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (18)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 548

Ala	Gln	Gly	Phe	Arg	His	Glu	Xaa	Xaa	Leu	Leu	Val	Gly	Gly	Leu	Leu
1				5					10					15	

Ala Xaa Asp Gly Asp Cys Pro Gly Val Val Thr Met Phe Leu Ser Ala
 20 25 30

Val Phe Phe Ala Lys Ser Lys Ser Lys Asn Ile Leu Val Arg Met Val
 35 40 45

Ser Glu Ala Gly Thr Gly Phe Cys Phe Asn Thr Lys Arg Asn Arg Leu
 50 55 60

Arg Glu Lys Leu Thr Leu Leu His Tyr Asp Pro Val Val Lys Gln Arg
 65 70 75 80

Val Leu Phe Val Glu Lys Lys Lys Ile Arg Ser Leu
 85 90

<210> 549

<211> 393

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (195)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (252)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 549

Gly Arg Gly Phe Lys Lys Asn Leu Phe Glu Met Ala Ile Asn Leu Ala
 1 5 10 15

Lys Ser Gln His Leu Asp Ser Asp Gly Leu Ala Gln Ile Phe Met Gln
 20 25 30

Tyr Gly Asp His Leu Tyr Ser Lys Gly Asn His Asp Gly Ala Val Gln
 35 40 45

Gln Tyr Ile Arg Thr Ile Gly Lys Leu Glu Pro Ser Tyr Val Ile Arg
 50 55 60

Lys Phe Leu Asp Ala Gln Arg Ile His Asn Leu Thr Ala Tyr Leu Gln
 65 70 75 80

Thr Leu His Arg Gln Ser Leu Ala Asn Ala Asp His Thr Thr Leu Leu
 85 90 95

Leu Asn Cys Tyr Thr Lys Leu Lys Asp Ser Ser Lys Leu Glu Glu Phe
100 105 110

Ile Lys Lys Lys Ser Glu Ser Glu Val His Phe Asp Val Glu Thr Ala
115 120 125

Ile Lys Val Leu Arg Gln Ala Gly Tyr Tyr Ser His Ala Leu Tyr Leu
130 135 140

Ala Glu Asn His Ala His His Glu Trp Tyr Leu Lys Ile Gln Leu Glu
145 150 155 160

Asp Ile Lys Asn Tyr Gln Glu Ala Leu Arg Tyr Ile Gly Lys Leu Pro
165 170 175

Phe Glu Gln Ala Glu Ser Asn Met Lys Arg Tyr Gly Lys Ile Leu Met
180 185 190

His His Xaa Pro Glu Gln Thr Thr Gln Leu Leu Lys Gly Leu Cys Thr
195 200 205

Asp Tyr Arg Pro Ser Leu Glu Gly Arg Ser Asp Arg Glu Ala Pro Gly
210 215 220

Cys Arg Ala Asn Ser Glu Glu Phe Ile Pro Ile Phe Ala Asn Asn Pro
225 230 235 240

Arg Glu Leu Lys Ala Phe Leu Glu His Met Ser Xaa Val Gln Pro Asp
245 250 255

Ser Pro Gln Gly Ile Tyr Asp Thr Leu Leu Glu Leu Arg Leu Gln Asn
260 265 270

Trp Ala His Glu Lys Asp Pro Gln Val Lys Glu Lys Leu His Ala Glu
275 280 285

Ala Ile Ser Leu Leu Lys Ser Gly Arg Phe Cys Asp Val Phe Asp Lys
290 295 300

Ala Leu Val Leu Cys Gln Met His Asp Phe Gln Asp Gly Val Leu Tyr
305 310 315 320

Leu Tyr Glu Gln Gly Lys Leu Phe Gln Gln Ile Met His Tyr His Met
325 330 335

Gln His Glu Gln Tyr Arg Gln Ser Ser Ala Cys Val Ser Ala Met Gly
340 345 350

Ser Arg Thr Pro Pro Cys Gly Ser Arg Pro Ser Ala Thr Ser Leu Ala
355 360 365

Arg Arg Arg Thr Ala Arg Ser Met Trp Gln Leu Ser Ser Ser Ile Ser
 370 375 380

Arg Thr Arg Thr Ser Cys His Leu Phe
 385 390

<210> 550

<211> 786

<212> PRT

<213> Homo sapiens

<400> 550

Arg Ser His Ser Val Tyr Ile Thr Ser Thr Val Leu Ala Pro Asn Val
 1 5 10 15

Leu Cys Val Leu Leu Leu Trp Leu Asn Pro Gln Ala Leu Val Gly Ala
 20 25 30

Gln Gly Gly Arg Met Ser Gln Trp Tyr Glu Leu Gln Gln Leu Asp Ser
 35 40 45

Lys Phe Leu Glu Gln Val His Gln Leu Tyr Asp Asp Ser Phe Pro Met
 50 55 60

Glu Ile Arg Gln Tyr Leu Ala Gln Trp Leu Glu Lys Gln Asp Trp Glu
 65 70 75 80

His Ala Ala Asn Asp Val Ser Phe Ala Thr Ile Arg Phe His Asp Leu
 85 90 95

Leu Ser Gln Leu Asp Asp Gln Tyr Ser Arg Phe Ser Leu Glu Asn Asn
 100 105 110

Phe Leu Leu Gln His Asn Ile Arg Lys Ser Lys Arg Asn Leu Gln Asp
 115 120 125

Asn Phe Gln Glu Asp Pro Ile Gln Met Ser Met Ile Ile Tyr Ser Cys
 130 135 140

Leu Lys Glu Glu Arg Lys Ile Leu Glu Asn Ala Gln Arg Phe Asn Gln
 145 150 155 160

Ala Gln Ser Gly Asn Ile Gln Ser Thr Val Met Leu Asp Lys Gln Lys
 165 170 175

Glu Leu Asp Ser Lys Val Arg Asn Val Lys Asp Lys Val Met Cys Ile
 180 185 190

Glu His Glu Ile Lys Ser Leu Glu Asp Leu Gln Asp Glu Tyr Asp Phe
 195 200 205
 Lys Cys Lys Thr Leu Gln Asn Arg Glu His Glu Thr Asn Gly Val Ala
 210 215 220
 Lys Ser Asp Gln Lys Gln Glu Gln Leu Leu Leu Lys Lys Met Tyr Leu
 225 230 235 240
 Met Leu Asp Asn Lys Arg Lys Glu Val Val His Lys Ile Ile Glu Leu
 245 250 255
 Leu Asn Val Thr Glu Leu Thr Gln Asn Ala Leu Ile Asn Asp Glu Leu
 260 265 270
 Val Glu Trp Lys Arg Arg Gln Gln Ser Ala Cys Ile Gly Gly Pro Pro
 275 280 285
 Asn Ala Cys Leu Asp Gln Leu Gln Asn Trp Phe Thr Ile Val Ala Glu
 290 295 300
 Ser Leu Gln Gln Val Arg Gln Gln Leu Lys Lys Leu Glu Glu Leu Glu
 305 310 315 320
 Gln Lys Tyr Thr Tyr Glu His Asp Pro Ile Thr Lys Asn Lys Gln Val
 325 330 335
 Leu Trp Asp Arg Thr Phe Ser Leu Phe Gln Gln Leu Ile Gln Ser Ser
 340 345 350
 Phe Val Val Glu Arg Gln Pro Cys Met Pro Thr His Pro Gln Arg Pro
 355 360 365
 Leu Val Leu Lys Thr Gly Val Gln Phe Thr Val Lys Leu Arg Leu Leu
 370 375 380
 Val Lys Leu Gln Glu Leu Asn Tyr Asn Leu Lys Val Lys Val Leu Phe
 385 390 395 400
 Asp Lys Asp Val Asn Glu Arg Asn Thr Val Lys Gly Phe Arg Lys Phe
 405 410 415
 Asn Ile Leu Gly Thr His Thr Lys Val Met Asn Met Glu Glu Ser Thr
 420 425 430
 Asn Gly Ser Leu Ala Ala Glu Phe Arg His Leu Gln Leu Lys Glu Gln
 435 440 445
 Lys Asn Ala Gly Thr Arg Thr Asn Glu Gly Pro Leu Ile Val Thr Glu
 450 455 460

Glu Leu His Ser Leu Ser Phe Glu Thr Gln Leu Cys Gln Pro Gly Leu
 465 470 475 480

Val Ile Asp Leu Glu Thr Thr Ser Leu Pro Val Val Val Ile Ser Asn
 485 490 495

Val Ser Gln Leu Pro Ser Gly Trp Ala Ser Ile Leu Trp Tyr Asn Met
 500 505 510

Leu Val Ala Glu Pro Arg Asn Leu Ser Phe Phe Leu Thr Pro Pro Cys
 515 520 525

Ala Arg Trp Ala Gln Leu Ser Glu Val Leu Ser Trp Gln Phe Ser Ser
 530 535 540

Val Thr Lys Arg Gly Leu Asn Val Asp Gln Leu Asn Met Leu Gly Glu
 545 550 555 560

Lys Leu Leu Gly Pro Asn Ala Ser Pro Asp Gly Leu Ile Pro Trp Thr
 565 570 575

Arg Phe Cys Lys Glu Asn Ile Asn Asp Lys Asn Phe Pro Phe Trp Leu
 580 585 590

Trp Ile Glu Ser Ile Leu Glu Leu Ile Lys Lys His Leu Leu Pro Leu
 595 600 605

Trp Asn Asp Gly Cys Ile Met Gly Phe Ile Ser Lys Glu Arg Glu Arg
 610 615 620

Ala Leu Leu Lys Asp Gln Gln Pro Gly Thr Phe Leu Leu Arg Phe Ser
 625 630 635 640

Glu Ser Ser Arg Glu Gly Ala Ile Thr Phe Thr Trp Val Glu Arg Ser
 645 650 655

Gln Asn Gly Gly Glu Pro Asp Phe His Ala Val Glu Pro Tyr Thr Lys
 660 665 670

Lys Glu Leu Ser Ala Val Thr Phe Pro Asp Ile Ile Arg Asn Tyr Lys
 675 680 685

Val Met Ala Ala Glu Asn Ile Pro Glu Asn Pro Leu Lys Tyr Leu Tyr
 690 695 700

Pro Asn Ile Asp Lys Asp His Ala Phe Gly Lys Tyr Tyr Ser Arg Pro
 705 710 715 720

Lys Glu Ala Pro Glu Pro Met Glu Leu Asp Gly Pro Lys Gly Thr Gly
 725 730 735

Tyr Ile Lys Thr Glu Leu Ile Ser Val Ser Glu Val His Pro Ser Arg
 740 745 750

Leu Gln Thr Thr Asp Asn Leu Leu Pro Met Ser Pro Glu Glu Phe Asp
 755 760 765

Glu Val Ser Arg Ile Val Gly Ser Val Glu Phe Asp Ser Met Met Asn
 770 775 780

Thr Val
 785

<210> 551

<211> 68

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (46)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 551

Gly Thr Ser Leu Arg Glu Ser Gln Arg Ser Leu Trp Gly Val Arg Leu
 1 5 10 15

Arg Gly Cys Pro Arg Thr Glu Pro Arg Ser Ala Ser Gly Glu Pro Arg
 20 25 30

Glu Val Gly Val Gly Pro Ala Ala Gly Gln Glu Pro Cys Xaa Leu Glu
 35 40 45

Asp Pro Pro Lys Arg Lys Gln Thr Leu Phe Phe Phe Ile Gln Pro Gln
 50 55 60

Ile Ala Arg Ala
 65

<210> 552

<211> 511

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (44)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (45)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (46)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (412)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (476)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (492)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (504)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 552
Asp Pro Gly Val Pro Gly Pro Glu Ala Gly His Glu Arg Ala Ala Glu
1 5 10 15
Arg Gly Glu Gly Val Pro Glu Gln Arg Gln Leu Arg Gly Glu Leu His
20 25 30
Pro Glu Tyr His Leu His Arg Gly Ala Gly Ala Xaa Xaa Xaa Ala Thr
35 40 45
Leu Val Val Gly Gly Asp Gly Arg Phe Tyr Met Lys Glu Ala Ile Gln
50 55 60
Leu Ile Ala Arg Ile Ala Ala Ala Asn Gly Ile Gly Arg Leu Val Ile
65 70 75 80
Gly Gln Asn Gly Ile Leu Ser Thr Pro Ala Val Ser Cys Ile Ile Arg
85 90 95
Lys Ile Lys Ala Ile Gly Gly Ile Ile Leu Thr Ala Ser His Asn Pro

100	105	110
Gly Gly Pro Asn Gly Asp Phe Gly Ile Lys Phe Asn Ile Ser Asn Gly 115	120	125
Gly Pro Ala Pro Glu Ala Ile Thr Asp Lys Ile Phe Gln Ile Ser Lys 130	135	140
Thr Ile Glu Glu Tyr Ala Val Cys Pro Asp Leu Lys Val Asp Leu Gly 145	150	155 160
Val Leu Gly Lys Gln Gln Phe Asp Leu Glu Asn Lys Phe Lys Pro Phe 165	170	175
Thr Val Glu Ile Val Asp Ser Val Glu Ala Tyr Ala Thr Met Leu Arg 180	185	190
Ser Ile Phe Asp Phe Ser Ala Leu Lys Glu Leu Leu Ser Gly Pro Asn 195	200	205
Arg Leu Lys Ile Arg Ile Asp Ala Met His Gly Val Val Gly Pro Tyr 210	215	220
Val Lys Lys Ile Leu Cys Glu Glu Leu Gly Ala Pro Ala Asn Ser Ala 225	230	235 240
Val Asn Cys Val Pro Leu Glu Asp Phe Gly Gly His His Pro Asp Pro 245	250	255
Asn Leu Thr Tyr Ala Ala Asp Leu Val Glu Thr Met Lys Ser Gly Glu 260	265	270
His Asp Phe Gly Ala Ala Phe Asp Gly Asp Gly Asp Arg Asn Met Ile 275	280	285
Leu Gly Lys His Gly Phe Phe Val Asn Pro Ser Asp Ser Val Ala Val 290	295	300
Ile Ala Ala Asn Ile Phe Ser Ile Pro Tyr Phe Gln Gln Thr Gly Val 305	310	315 320
Arg Gly Phe Ala Arg Ser Met Pro Thr Ser Gly Ala Leu Asp Arg Val 325	330	335
Ala Ser Ala Thr Lys Ile Ala Leu Tyr Glu Thr Pro Thr Gly Trp Lys 340	345	350
Phe Phe Gly Asn Leu Met Asp Ala Ser Lys Leu Ser Leu Cys Gly Glu 355	360	365
Glu Ser Phe Gly Thr Gly Ser Asp His Ile Arg Glu Lys Asp Gly Leu		

495

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370          375          380
Trp Ala Val Leu Ala Trp Leu Ser Ile Leu Ala Thr Arg Lys Gln Ser
385          390          395          400
Val Glu Asp Ile Leu Lys Asp His Trp Gln Lys Xaa Gly Arg Asn Phe
          405          410          415
Phe Thr Arg Tyr Asp Tyr Glu Glu Val Glu Ala Glu Gly Ala Asn Lys
          420          425          430
Met Met Lys Asp Leu Glu Ala Leu Met Phe Asp Arg Ser Phe Val Gly
          435          440          445
Lys Gln Phe Ser Ala Asn Asp Lys Val Tyr Thr Val Glu Lys Ala Asp
          450          455          460
Asn Phe Glu Tyr Ser Asp Pro Val Asp Gly Ser Xaa Ser Arg Asn Gln
465          470          475          480
Gly Leu Arg Leu Ile Phe Thr Asp Gly Ser Arg Xaa Arg Leu Pro Thr
          485          490          495
Glu Arg His Trp Glu Cys Gly Xaa His His Ser Ala Val His Arg
          500          505          510

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<210> 553
 <211> 184
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (118)
 <223> Xaa equals any of the naturally occurring L-amino acids

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<400> 553
Gln Pro Ser Pro His Ser Gln Ser Arg Pro Ser Pro Gln Lys Asp Pro
 1              5              10              15
Gln Pro Leu Leu Leu Pro Arg Leu Asp Pro Gly Gln Arg Gly Asn Lys
          20              25              30
Leu Pro Thr Gly Glu Gln Gly Leu Asp Glu Asp Val Asp Gly Val Cys
          35              40              45
Glu Ser His Ala Ala Pro Gly Leu Glu Cys Ser Ser Gly Ser Ala Asn
          50              55              60

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Cys Gln Gly Ala Gly Pro Ser Ala Asp Gly Ile Ser Ser Arg Leu Thr
 65 70 75 80
 Pro Ala Glu Ser Cys Met Gly Leu Val Arg Met Asn Leu Tyr Thr His
 85 90 95
 Cys Val Lys Gly Leu Met Leu Ser Leu Leu Ala Glu Glu Pro Leu Leu
 100 105 110
 Gly Asp Ser Ala Pro Xaa Glu Glu Val Tyr His Ser Ser Leu Ala Ser
 115 120 125
 Leu Asn Gly Leu Glu Val His Leu Lys Glu Thr Leu Pro Arg Asp Glu
 130 135 140
 Ala Ala Ser Thr Ser Ser Thr Tyr Asn Phe Thr Tyr Tyr Asp Arg Ile
 145 150 155 160
 Gln Ser Leu Leu Met Ala Asn Leu Pro Gln Trp Pro Pro Arg Met Ile
 165 170 175
 Ala Ala Ser Ser Arg Pro Ser Ala
 180

<210> 554

<211> 80

<212> PRT

<213> Homo sapiens

<400> 554

Ala Arg Ala Val Gly Tyr Leu Thr Thr Pro Thr Ala Ala Leu Ala Ser
 1 5 10 15
 Ala Pro Thr Ser Val Leu Ser Gln Ser Gly Ala Leu Val Arg Met Gln
 20 25 30
 Gly Val Pro Tyr Thr Ala Gly Met Lys Asp Leu Leu Ser Val Phe Gln
 35 40 45
 Ala Tyr Gln Leu Pro Ala Asp Asp Tyr Thr Ser Leu Met Pro Val Gly
 50 55 60
 Asp Pro Pro Arg Thr Val Leu Gln Ala Pro Lys Glu Trp Val Cys Leu
 65 70 75 80

<210> 555
<211> 141
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (136)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 555
Gly His Glu Leu Glu Thr Thr Ala Asp Val Glu Glu Ile Thr Gly Glu
1 5 10 15
Gly Leu Thr Ala Ser Gly Ser Gly Asp Val Met Arg Arg Arg Ile Ala
20 25 30
Thr Pro Glu Glu Val Arg Leu Pro Leu Gln His Gly Trp Arg Arg Glu
35 40 45
Val Arg Ile Lys Lys Gly Ser His Arg Trp Gln Gly Glu Thr Trp Tyr
50 55 60
Tyr Gly Pro Cys Gly Lys Arg Met Lys Gln Phe Pro Glu Val Ile Lys
65 70 75 80
Tyr Leu Ser Arg Asn Val Val His Ser Val Arg Arg Glu His Phe Ser
85 90 95
Phe Ser Pro Arg Met Pro Val Gly Asp Phe Phe Glu Arg Lys Arg His
100 105 110
Ala Arg Gly Ala Asp Pro Lys Val Lys Tyr Ala Phe Val Pro Glu Glu
115 120 125
Glu Leu Val Asp Lys Leu Gln Xaa Pro Leu Val Gly Val
130 135 140

<210> 556
<211> 110
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 556

Glu Ser Met Asn Ile Phe Glu Thr Ile Val Asn Asn Lys Leu Phe Phe
1 5 10 15
Asn Val Ser Ile Ile Leu Phe Leu Asn Lys Met Asp Leu Leu Val Glu
20 25 30
Lys Val Lys Thr Val Ser Ile Lys Lys His Phe Pro Asp Phe Arg Gly
35 40 45
Asp Pro His Arg Leu Glu Asp Val Gln Arg Tyr Leu Val Gln Cys Phe
50 55 60
Asp Arg Lys Arg Arg Asn Arg Ser Lys Pro Leu Phe His His Phe Thr
65 70 75 80
Thr Ala Ile Asp Thr Glu Asn Val Arg Phe Val Phe His Ala Val Lys
85 90 95
Asp Thr Ile Leu Gln Glu Asn Leu Xaa Asp Ile Met Leu Gln
100 105 110

<210> 557

<211> 99

<212> PRT

<213> Homo sapiens

<400> 557

Lys Ser Asn Lys Asn Ile Leu Phe Ile Ile Ala Leu Cys Phe Gly Leu
1 5 10 15
Cys Arg Pro Pro Asp Thr His Glu Ala Pro Thr Ser Gln Ala Gly Lys
20 25 30
Ala Lys Ser Leu Pro Ser Ala Phe Leu Val Met Leu His Leu Ala Glu
35 40 45
Cys Leu Gln Gly Leu Asp Pro Ser Ala Leu Arg His Ser Trp Ala Lys
50 55 60
Gln Lys Glu Arg Asn Thr Ser Ala Val Thr Leu Asn Glu Leu Arg Asn
65 70 75 80
Ser Phe Pro Leu Asp Cys Arg Gly Ala Asn Cys Leu Glu Gln Lys Thr
85 90 95
Ala Gly Cys

<210> 558
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 558
Phe Xaa Pro Leu Pro Phe Phe Phe Phe Leu Ser Pro Ser Gly Gly Ile
1 5 10 15

Pro Glu Glu Gly Ile Val Val Met Gly Asp Asn Ser Ser Met His Val
20 25 30

Ile Ala Pro Glu Asp Leu Pro Val Lys Arg Asp Val Glu Val Glu Asp
35 40 45

Ser Asp Ile
50

<210> 559
<211> 160
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (138)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (152)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (158)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 559
Thr His Ala Ser Gly Arg Gly Cys Cys Gly Arg Val Arg Leu Leu Arg
1 5 10 15

500

Arg Gly Leu His Val Asp Cys Gly Lys Leu Gly Asn Lys Leu Thr Ser
 20 25 30
 Ser Cys Gly Lys Pro Ser Ser Asn Arg Met Ser Leu Gln Trp Thr Ala
 35 40 45
 Val Ala Thr Phe Leu Tyr Ala Glu Val Phe Val Val Leu Leu Leu Cys
 50 55 60
 Ile Pro Phe Ile Ser Pro Lys Arg Trp Gln Lys Ile Phe Lys Ser Arg
 65 70 75 80
 Leu Val Glu Leu Leu Val Ser Tyr Gly Asn Thr Phe Phe Val Val Leu
 85 90 95
 Ile Val Ile Leu Val Leu Leu Val Ile Asp Ala Val Arg Glu Ile Arg
 100 105 110
 Lys Tyr Asp Asp Val Thr Glu Lys Val Asn Leu Gln Asn Asn Pro Gly
 115 120 125
 Ala Met Glu His Phe His Met Lys Leu Xaa Pro Cys Pro Glu Glu Ser
 130 135 140
 Leu Thr Leu Ala Gly Phe Ser Xaa Trp Cys Pro Pro Val Xaa Ser Pro
 145 150 155 160

<210> 560

<211> 81

<212> PRT

<213> Homo sapiens

<400> 560

Trp Arg Ser Arg Arg Met Glu Glu Leu Arg Met Leu Glu Glu Glu
 1 5 10 15
 Asn Gln Gly Gly Gly Ser Asp Met Pro Trp Arg Leu Val Gly Ser Gly
 20 25 30
 Leu Glu Gly Gly Gln Ala Gly Ser Gly Arg Pro Trp Glu Lys Trp Arg
 35 40 45
 Glu Val Ser Gly Gly Leu Ala Ser Ala Ala Ala Pro Trp Trp Val Pro
 50 55 60
 Gly Leu Ala Thr Ala Arg Ala Gly Arg Gly Glu Gly Arg Gly Leu Pro

501

65

70

75

80

Asn

<210> 561

<211> 67

<212> PRT

<213> Homo sapiens

<400> 561

Gln Leu Thr Gly Cys Arg His Gly Arg Gly Phe Leu Lys Ile Ser Leu
1 5 10 15

Ser Ile Thr Ile Ser Ile Phe Thr Phe Glu Asn Leu Leu Trp Arg Leu
20 25 30

Arg Thr Ser Lys Leu Leu Thr Tyr Phe Leu Tyr Lys Val Thr Pro Met
35 40 45

Lys Gly Asp Tyr Lys Ile Ile Tyr Ile Ala Val Tyr Lys Thr Asp Asn
50 55 60

Met Asp Val
65

<210> 562

<211> 87

<212> PRT

<213> Homo sapiens

<400> 562

Arg Ile His Glu Lys Tyr Glu Ile Trp Phe His Pro Val Arg His Phe
1 5 10 15

Asn Arg Glu Asp Gln Asn Val Thr Trp Gln Leu Gly Asn Asn Leu Thr
20 25 30

Ser Leu Ala Val Gly Leu Asn Phe Leu Ile Ile Asp Pro Gly Ile Phe
35 40 45

Gln Pro Glu Thr Gln Leu Ser Gly Arg Gln Thr Asn Cys Thr Thr Pro
50 55 60

Thr Ile Ser Trp Thr Leu Lys Phe Cys Leu Leu Gln Ser Ile Val Ser
65 70 75 80

Phe Lys Ala Pro Val Leu Ala
85

<210> 563
<211> 123
<212> PRT
<213> Homo sapiens

<400> 563
His Phe Leu Gln Pro Ser Leu Ser Gln Ile Cys His Ile Gly Leu Pro
1 5 10 15

Phe Gln Pro Arg His Leu Thr Arg Ala Ile Cys Cys Arg Val Thr Arg
20 25 30

Asp Gly Ser Ala Phe Glu Asp Gly Leu Arg His Pro Phe Ile Val Asn
35 40 45

His Pro Lys Val Gly Arg Val Ser Ile Tyr Asp Ser Lys Arg Gln Ser
50 55 60

Gly Lys Thr Lys Glu Thr Ser Val Asn Trp Cys Leu Ala Asp Gly Tyr
65 70 75 80

Asp Leu Glu Ile Leu Asp Gly Thr Arg Gly Thr Val Asp Gly Pro Arg
85 90 95

Asn Glu Leu Ser Arg Val Ser Lys Lys Asn Ile Phe Leu Leu Phe Lys
100 105 110

Lys Leu Cys Ser Phe Arg Tyr Arg Arg Ile Tyr
115 120

<210> 564
<211> 188
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (117)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 564
Tyr Val Met Glu Ser Arg Asp Pro Ser Thr Asn Val Ile Leu Leu Glu
1 5 10 15

Asp Thr Ala Ala Val Leu Gly Val Ile Ile Ala Ala Thr Cys Met Gly
20 25 30

Leu Thr Ser Ile Thr Gly Asn Pro Leu Tyr Asp Ser Leu Gly Ser Leu
35 40 45

Gly Val Gly Thr Leu Leu Gly Met Val Ser Ala Phe Leu Ile Tyr Thr
50 55 60

Asn Thr Glu Ala Leu Leu Gly Arg Ser Ile Gln Pro Glu Gln Val Gln
65 70 75 80

Arg Leu Thr Glu Leu Leu Glu Asn Asp Pro Ser Val Arg Ala Ile His
85 90 95

Asp Val Lys Ala Thr Asp Leu Gly Leu Gly Lys Val Arg Phe Lys Ala
100 105 110

Glu Val Asp Phe Xaa Gly Arg Val Val Thr Arg Ser Tyr Leu Glu Lys
115 120 125

Gln Asp Phe Asp Gln Met Leu Gln Glu Ile Gln Glu Val Lys Thr Pro
130 135 140

Glu Glu Leu Glu Thr Phe Met Leu Lys His Gly Glu Asn Ile Ile Asp
145 150 155 160

Thr Leu Gly Ala Glu Val Asp Arg Leu Glu Lys Glu Leu Lys Lys Arg
165 170 175

Asn Pro Glu Val Arg His Val Asp Leu Glu Ile Leu
180 185

<210> 565

<211> 71

<212> PRT

<213> Homo sapiens

<400> 565

Asp Val Ile Ser Met Glu Leu Arg Phe Asp Phe Ser His Ser Leu Thr
1 5 10 15

His Arg Arg Arg Thr Lys Glu Arg Asn Glu Ile Met Leu Thr Met Lys
20 25 30

Leu Phe Ile Thr Ser Thr Asp Leu Ser Leu Ser Leu Phe Leu Ser Phe
35 40 45

Ser Phe Ser His Thr Pro Arg Gln Asn Phe Phe Lys Glu Met Thr Leu

<220>

<221> SITE

<222> (237)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (238)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (243)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 611

Glu	Gly	Glu	Lys	Ile	Ser	Ala	Asn	Glu	Asn	Ser	Leu	Ala	Val	Arg	Ser
1				5					10					15	

Thr	Pro	Ala	Glu	Asp	Asp	Ser	Arg	Asp	Ser	Gln	Val	Lys	Ser	Glu	Val
			20					25					30		

Gln	Gln	Pro	Val	His	Pro	Lys	Pro	Leu	Ser	Pro	Asp	Ser	Arg	Ala	Ser
		35				40						45			

Ser	Leu	Ser	Glu	Ser	Ser	Pro	Pro	Lys	Ala	Met	Lys	Lys	Phe	Gln	Ala
50						55					60				

Pro	Ala	Arg	Glu	Thr	Cys	Val	Glu	Cys	Gln	Lys	Thr	Val	Tyr	Pro	Met
65					70					75					80

Glu	Arg	Leu	Leu	Ala	Asn	Gln	Gln	Val	Phe	His	Ile	Ser	Cys	Phe	Arg
				85				90						95	

Cys	Ser	Tyr	Cys	Asn	Asn	Lys	Leu	Ser	Leu	Gly	Thr	Tyr	Ala	Ser	Leu
			100					105					110		

His	Gly	Arg	Ile	Tyr	Cys	Lys	Pro	His	Phe	Asn	Gln	Leu	Phe	Lys	Ser
			115				120					125			

Lys	Gly	Asn	Tyr	Asp	Glu	Gly	Phe	Gly	His	Arg	Pro	His	Lys	Asp	Leu
	130					135					140				

Trp	Ala	Ser	Lys	Asn	Glu	Asn	Glu	Glu	Ile	Leu	Glu	Arg	Pro	Ala	Gln
145					150					155					160

Leu	Ala	Asn	Ala	Arg	Glu	Thr	Pro	His	Ser	Pro	Gly	Val	Glu	Asp	Ala
				165					170					175	

Pro	Ile	Ala	Lys	Val	Gly	Val	Leu	Xaa	Ala	Ser	Met	Glu	Ala	Lys	Ala
			180					185						190	

Lys Leu Glu Asp Lys Leu Asn Arg His Leu Ser Cys Asp Leu Met Pro
435 440 445

Asn Glu Asn Ile Pro Glu Leu Ala Ala Glu Leu Val Gln Leu Gly Phe
450 455 460

Ile Ser Glu Ala Asp Gln Ser Arg Leu Thr Ser Leu Leu Glu Glu Thr
465 470 475 480

Leu Asn Lys Phe Asn Phe Ala Arg Asn Ser Thr Leu Asn Ser Ala Ala
485 490 495

Val Thr Val Ser Ser
500

<210> 610
<211> 77
<212> PRT
<213> Homo sapiens

<400> 610
Gly Arg Val Gly Phe Ile Ile Leu Ser Trp His Ser Ser Lys Arg Thr
1 5 10 15

Leu Arg Trp Glu Leu Trp Gly Thr Gly Arg Arg Gly Gln Leu Gly Thr
20 25 30

Gly Pro Val Gly Val Ala Val Trp Gly Met Gly Val Cys Ser Leu Ala
35 40 45

Leu Val Leu Gly Gly Met Arg Val Lys Lys Gly Arg Gly Leu Val Arg
50 55 60

Asp Thr Val Trp Val Val Gly Val Val Gly Asn Ala Gly
65 70 75

<210> 611
<211> 243
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (185)
<223> Xaa equals any of the naturally occurring L-amino acids

Asp Pro Pro Ile Ile His Gly Asn Leu Thr Cys Asp Thr Ile Phe Ile
 165 170 175

Gln His Asn Gly Leu Ile Lys Ile Gly Ser Val Ala Pro Asp Thr Ile
 180 185 190

Asn Asn His Val Lys Thr Cys Arg Glu Glu Gln Lys Asn Leu His Phe
 195 200 205

Phe Ala Pro Glu Tyr Gly Glu Val Thr Asn Val Thr Thr Ala Val Asp
 210 215 220

Ile Tyr Ser Phe Gly Met Cys Ala Leu Glu Met Ala Val Leu Glu Ile
 225 230 235 240

Gln Gly Asn Gly Glu Ser Ser Tyr Val Pro Gln Glu Ala Ile Ser Ser
 245 250 255

Ala Ile Gln Leu Leu Glu Asp Pro Leu Gln Arg Glu Phe Ile Gln Lys
 260 265 270

Cys Leu Gln Ser Glu Pro Ala Arg Arg Pro Thr Ala Arg Glu Leu Leu
 275 280 285

Phe His Pro Ala Leu Phe Glu Val Pro Ser Leu Lys Leu Leu Ala Ala
 290 295 300

His Cys Ile Val Gly His Gln His Met Ile Pro Glu Asn Ala Leu Glu
 305 310 315 320

Glu Ile Thr Lys Asn Met Asp Thr Ser Ala Val Leu Ala Glu Ile Pro
 325 330 335

Ala Gly Pro Gly Arg Glu Pro Val Gln Thr Leu Tyr Ser Gln Ser Pro
 340 345 350

Ala Leu Glu Leu Asp Lys Phe Leu Glu Asp Val Arg Asn Gly Ile Tyr
 355 360 365

Pro Leu Thr Ala Phe Gly Leu Pro Arg Pro Gln Gln Pro Gln Gln Glu
 370 375 380

Glu Val Thr Ser Pro Val Val Pro Pro Ser Val Lys Thr Pro Thr Pro
 385 390 395 400

Glu Pro Ala Glu Val Glu Thr Arg Lys Val Val Leu Met Gln Cys Asn
 405 410 415

Ile Glu Ser Val Glu Glu Gly Val Lys His His Leu Thr Leu Leu Leu
 420 425 430

550

Thr Phe Ser Cys Phe Lys Thr Ser Trp Phe
 370 375

<210> 609
 <211> 501
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (29)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (30)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 609
 Pro Pro Gln Pro Gln Leu Leu Pro Gln Arg Lys Lys Lys Lys Val Lys
 1 5 10 15
 Met Ser Leu Arg Phe Trp Lys Ser Arg Pro Val Gly Xaa Xaa Gln Lys
 20 25 30
 Arg Arg Glu Glu Val Asn Gln Arg Asn Val Pro Gly Ile Asp Ser Ala
 35 40 45
 Tyr Leu Ala Met Asp Thr Glu Glu Gly Val Glu Val Val Trp Asn Glu
 50 55 60
 Val Gln Phe Ser Glu Arg Lys Asn Tyr Lys Leu Gln Glu Glu Lys Val
 65 70 75 80
 Arg Ala Val Phe Asp Asn Leu Ile Gln Leu Glu His Leu Asn Ile Val
 85 90 95
 Lys Phe His Lys Tyr Trp Ala Asp Ile Lys Glu Asn Lys Ala Arg Val
 100 105 110
 Ile Phe Ile Thr Glu Tyr Met Ser Ser Gly Ser Leu Lys Gln Phe Leu
 115 120 125
 Lys Lys Thr Lys Lys Asn His Lys Thr Met Asn Glu Lys Ala Trp Lys
 130 135 140
 Arg Trp Cys Thr Gln Ile Leu Ser Ala Leu Ser Tyr Leu His Ser Cys
 145 150 155 160

Arg Ser Pro Ala Ser Ala Gln Lys Phe Ser Ser Arg Ser Thr Val Pro
100 105 110

Thr Pro Ala Lys Arg Arg Ser Ser Ala Leu Trp Ser Glu Met Leu Asp
115 120 125

Ile Thr Met Lys Glu Ser Leu Thr Thr Arg Glu Ile Arg Arg Gln Glu
130 135 140

Ala Ile Tyr Glu Met Ser Arg Gly Glu Gln Asp Leu Ile Glu Asp Leu
145 150 155 160

Lys Leu Ala Arg Lys Ala Tyr His Asp Pro Met Leu Lys Leu Ser Ile
165 170 175

Met Ser Glu Glu Glu Leu Thr His Ile Phe Gly Asp Leu Asp Ser Tyr
180 185 190

Ile Pro Leu His Glu Asp Leu Leu Thr Arg Ile Gly Glu Ala Thr Lys
195 200 205

Pro Asp Gly Thr Val Glu Gln Ile Gly His Ile Leu Val Ser Trp Leu
210 215 220

Pro Arg Leu Asn Ala Tyr Arg Gly Tyr Cys Ser Asn Gln Leu Ala Ala
225 230 235 240

Lys Ala Leu Leu Asp Gln Lys Lys Gln Asp Pro Arg Val Gln Asp Phe
245 250 255

Leu Gln Arg Cys Leu Glu Ser Pro Phe Ser Arg Lys Leu Asp Leu Trp
260 265 270

Ser Phe Leu Asp Ile Pro Arg Ser Arg Leu Val Lys Tyr Pro Leu Leu
275 280 285

Leu Lys Glu Ile Leu Lys His Thr Pro Lys Glu His Pro Asp Val Gln
290 295 300

Leu Leu Glu Asp Ala Ile Leu Ile Ile Gln Gly Val Leu Ser Asp Ile
305 310 315 320

Asn Leu Lys Lys Gly Glu Ser Glu Cys Gln Tyr Tyr Ile Asp Lys Leu
325 330 335

Glu Tyr Leu Asp Glu Lys Gln Arg Asp Pro Arg Ile Glu Ala Ser Lys
340 345 350

Val Leu Leu Cys His Gly Glu Leu Arg Thr Arg Val Asp Ile Asn Phe
355 360 365

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      1             5             10             15
Pro Leu Tyr Leu Gly Asp Pro Ser Xaa Cys Thr Leu Leu Thr Asn Gly
      20             25             30
Trp Ser Ala Gly Glu Lys Ser Leu Cys Arg Pro Pro Ser Lys Pro Ser
      35             40             45
Val Cys Ala His Gly Ile Ser Lys Met Gly His Cys Cys Val Gln Asn
      50             55             60
Pro Gly Ser Ser Phe Cys Leu Gln Leu Leu Ser Leu Asp Ala Pro Glu
      65             70             75             80
Thr Ile Gln Ala Ser Phe Pro Ile Leu Pro Leu Cys Phe Ala Phe Tyr
      85             90             95
Pro Ser Thr Ser Ile Thr Ala Phe Ser Ser Phe Gln Asn Ser Leu Phe
      100            105            110
Leu Xaa Leu Phe Phe Met Ile Thr Lys Leu Leu Leu Pro Pro Trp Lys
      115            120            125
Ile Thr Ala Ile Asp Ala Cys Met
      130            135

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<210> 608

<211> 378

<212> PRT

<213> Homo sapiens

<400> 608

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Arg Arg Tyr Ser Ala Asp Ser Val Trp Ile Asp Trp Lys Gly Leu Arg
  1             5             10             15
Glu Tyr Leu Gly Ser Met Val Ala His Asp Glu Thr Gly Gly Leu Leu
      20             25             30
Pro Ile Lys Arg Thr Ile Arg Val Leu Asp Val Asn Asn Gln Ser Phe
      35             40             45
Arg Glu Gln Glu Glu Pro Ser Asn Lys Arg Val Arg Pro Leu Ala Arg
      50             55             60
Val Thr Ser Leu Ala Asn Leu Ile Ser Pro Val Arg Asn Gly Ala Val
      65             70             75             80
Arg Arg Phe Gly Gln Thr Ile Gln Ser Phe Thr Leu Arg Gly Asp His
      85             90             95

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Ser Gln Ser Asp Lys Thr Pro Glu Glu Leu Phe His Pro Leu Gly Ala
195 200 205

Asp Ser Gln Val
210

<210> 606
<211> 83
<212> PRT
<213> Homo sapiens

<400> 606
Asn Gln Glu Leu Thr Phe Pro Gly Cys Arg Val Ser Ile Pro Pro Phe
1 5 10 15

Leu Met Thr Ser Arg Met Phe Leu Thr Arg Lys Pro Thr Thr Phe Pro
20 25 30

Glu Ser Pro Ser Ser Trp Trp Val Glu Lys Cys Ser Pro Arg Cys Ala
35 40 45

Trp Phe Pro Ser His Val Pro Val Phe Lys Asp Ser Phe Thr Leu Val
50 55 60

Ser Glu Leu Lys Cys Cys Leu Leu Lys Gly Phe Gln Glu Arg Leu Cys
65 70 75 80

Lys Gly Leu

<210> 607
<211> 136
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (114)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 607
Ala Ala Gly Leu Val Ala Val Leu Ala Thr Val Ser Tyr Leu Pro Val

595

<210> 605

<211> 212

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (76)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 605

Ala Pro Thr Val Ser Leu Val Trp Gln Val Phe Tyr Tyr Ser Thr Ser
1 5 10 15

Ile Phe Glu Lys Ala Gly Val Gln Gln Pro Val Tyr Ala Thr Ile Gly
20 25 30

Ser Gly Ile Val Asn Thr Ala Phe Thr Val Val Ser Leu Phe Val Val
35 40 45

Glu Arg Ala Gly Arg Arg Thr Leu His Leu Ile Gly Leu Ala Gly Met
50 55 60

Ala Gly Cys Ala Ile Leu Met Thr Ile Ala Leu Xaa Leu Leu Glu Gln
65 70 75 80

Leu Pro Trp Met Ser Tyr Leu Ser Ile Val Ala Ile Phe Gly Phe Val
85 90 95

Ala Phe Phe Glu Val Gly Pro Gly Pro Ile Pro Trp Phe Ile Val Ala
100 105 110

Glu Leu Phe Ser Gln Gly Pro Arg Pro Ala Ala Ile Ala Val Ala Gly
115 120 125

Phe Ser Asn Trp Thr Ser Asn Phe Ile Val Gly Met Cys Phe Gln Tyr
130 135 140

Val Glu Gln Leu Cys Gly Pro Tyr Val Phe Ile Ile Phe Thr Val Leu
145 150 155 160

Leu Val Leu Phe Phe Ile Phe Thr Tyr Phe Lys Val Pro Glu Thr Lys
165 170 175

Gly Arg Thr Phe Asp Glu Ile Ala Ser Gly Phe Arg Gln Gly Gly Ala
180 185 190

545

	325		330		335
Leu Glu Glu Ser Ser Pro Ile Ala Ala Ile Phe Asp Thr Glu Asn Leu					
	340		345		350
Glu Lys Ile Ser Ile Thr Glu Gly Ile Glu Arg Gly Ile Val Asp Ser					
	355		360		365
Ile Thr Gly Gln Arg Leu Leu Glu Ala Gln Ala Cys Thr Gly Gly Ile					
	370		375		380
Ile His Pro Thr Thr Gly Gln Lys Leu Ser Leu Gln Asp Ala Val Ser					
	385		390		395
Gln Gly Val Ile Asp Gln Asp Met Ala Thr Arg Leu Lys Pro Ala Gln					
		405		410	415
Lys Ala Phe Ile Gly Phe Glu Gly Val Lys Gly Lys Lys Lys Met Ser					
	420		425		430
Ala Ala Glu Ala Val Lys Glu Lys Trp Leu Pro Tyr Glu Ala Gly Gln					
	435		440		445
Arg Phe Leu Glu Phe Gln Tyr Leu Thr Gly Gly Leu Val Asp Pro Glu					
	450		455		460
Val His Gly Arg Ile Ser Thr Glu Glu Ala Ile Arg Lys Gly Phe Ile					
	465		470		475
Asp Gly Arg Ala Ala Gln Arg Leu Gln Asp Thr Ser Ser Tyr Ala Lys					
		485		490	495
Ile Leu Thr Cys Pro Lys Thr Lys Leu Lys Ile Ser Tyr Lys Asp Ala					
	500		505		510
Ile Asn Arg Ser Met Val Glu Asp Ile Thr Gly Leu Arg Leu Leu Glu					
	515		520		525
Ala Ala Ser Val Ser Ser Lys Gly Leu Pro Ser Pro Tyr Asn Met Ser					
	530		535		540
Ser Ala Pro Gly Ser Arg Xaa Gly Ser Arg Ser Gly Ser Arg Ser Gly					
	545		550		555
Ser Arg Ser Gly Ser Arg Ser Gly Ser Arg Arg Gly Ser Phe Asp Ala					
		565		570	575
Thr Gly Asn Ser Ser Tyr Ser Tyr Ser Tyr Ser Phe Ser Ser Ser Ser					
	580		585		590
Ile Gly His					

50	55	60
Asp Pro Glu Thr Gly Asn Ile Ile Ser Leu Phe Gln Ala Met Asn Lys		
65	70	75 80
Glu Leu Ile Glu Lys Gly His Gly Ile Arg Leu Leu Glu Ala Gln Ile		
	85	90 95
Ala Thr Gly Gly Ile Ile Asp Pro Lys Glu Ser His Arg Leu Pro Val		
	100	105 110
Asp Ile Ala Tyr Lys Arg Gly Tyr Phe Asn Glu Glu Leu Ser Glu Ile		
	115	120 125
Leu Ser Asp Pro Ser Asp Asp Thr Lys Gly Phe Phe Asp Pro Asn Thr		
	130	135 140
Glu Glu Asn Leu Thr Tyr Leu Gln Leu Lys Glu Arg Cys Ile Lys Asp		
	145	150 155 160
Glu Glu Thr Gly Leu Cys Leu Leu Pro Leu Lys Glu Lys Lys Lys Gln		
	165	170 175
Val Gln Thr Ser Gln Lys Asn Thr Leu Arg Lys Arg Arg Val Val Ile		
	180	185 190
Val Asp Pro Glu Thr Asn Lys Glu Met Ser Val Gln Glu Ala Tyr Lys		
	195	200 205
Lys Gly Leu Ile Asp Tyr Glu Thr Phe Lys Glu Leu Cys Glu Gln Glu		
	210	215 220
Cys Glu Trp Glu Glu Ile Thr Ile Thr Gly Ser Asp Gly Ser Thr Arg		
	225	230 235 240
Val Val Leu Val Asp Arg Lys Thr Gly Ser Gln Tyr Asp Ile Gln Asp		
	245	250 255
Ala Ile Asp Lys Gly Leu Val Asp Arg Lys Phe Phe Asp Gln Tyr Arg		
	260	265 270
Ser Gly Ser Leu Ser Leu Thr Gln Phe Ala Asp Met Ile Ser Leu Lys		
	275	280 285
Asn Gly Val Gly Thr Ser Ser Ser Met Gly Ser Gly Val Ser Asp Asp		
	290	295 300
Val Phe Ser Ser Ser Arg His Glu Ser Val Ser Lys Ile Ser Thr Ile		
	305	310 315 320
Ser Ser Val Arg Asn Leu Thr Ile Arg Ser Ser Ser Phe Ser Asp Thr		

100	105	110
Cys Leu Glu Gln Pro Pro Tyr Ser Ser Leu Ala Gly Lys Glu Gly Thr		
115	120	125

<210> 604
 <211> 595
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (18)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (25)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (46)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (57)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (551)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 604
Gly His Glu Asn Trp Leu Ser Pro Thr Trp Tyr Cys Ser Gly Val Ala
1 5 10 15

Gly Xaa Gln Ala Ala Thr Gly Phe Xaa Val Asp Pro Val Ser Asn Leu
20 25 30

Arg Leu Pro Val Glu Glu Ala Tyr Lys Arg Gly Leu Val Xaa Ile Glu
35 40 45

Phe Lys Glu Lys Leu Leu Ser Ala Xaa Arg Ala Val Thr Gly Tyr Asn

Ser Thr Ser Leu Gly Leu Val Trp Leu Leu Lys Glu Arg Gly Ile Ser
 85 90 95
 Ala Ala Val Tyr Asp Pro Gln Ser Trp Asp Arg Ala Gly Arg Gly Ser
 100 105 110
 Leu Leu His Ser Tyr Thr Pro Lys Met Ala Val Ile Pro Ser Thr Pro
 115 120 125
 Pro Asn Ser Pro Met Gln Thr Pro Thr Ser Ser Pro Pro Ser Phe Glu
 130 135 140
 Phe Lys Cys Thr Ser Pro Pro Tyr Asp Asn Phe Leu Ala Ser Lys Pro
 145 150 155 160
 Arg Arg Leu His Pro Xaa
 165

<210> 603

<211> 128

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (88)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 603

Pro Pro Ala Arg Ala Pro Glu Cys Ser Pro Ser Gly Ser Leu Leu Gly
 1 5 10 15
 Ser Pro Leu Trp Arg Pro Cys Pro Arg Val Leu Leu Pro Arg Gly Leu
 20 25 30
 Leu Cys Ile Arg Arg Leu Arg Leu Gln Gly Tyr Pro Ala Arg Leu Pro
 35 40 45
 Ser Pro Arg Ala Glu Phe Ala Leu Leu Pro Glu Ser Phe Glu Arg Arg
 50 55 60
 Thr Asn Phe Trp Gln Asp Gly Asn Leu Asp Glu Pro Val Arg Ser Arg
 65 70 75 80
 Thr Pro Leu Ile Ser Gln Ala Xaa Arg His Pro His Leu Leu Gly Lys
 85 90 95
 Glu Gly Arg Gln Leu Val Pro Asp Leu Gly Glu Gln Leu Gln Thr Ala

245 250 255
 Lys Ser Leu Arg Gln Ser Arg Ser Arg Ser Arg Ser Lys Ala Gly Gln
 260 265 270
 Gln Glu Pro Glu Gln Glu Pro Gln Gln Glu Gln Gly Gln Glu Glu Glu
 275 280 285
 Gln Glu Glu Lys Gln Arg Gly Glu Pro Gln Ser Gln Ser Gln Pro Gln
 290 295 300
 Gln Glu
 305

<210> 602
 <211> 166
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (9)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (56)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (166)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 602
 Arg Thr Ile Leu Gly Lys Cys Met Xaa Gln Thr Asn Ser Thr Phe Thr
 1 5 10 15
 Phe Thr Thr Cys Arg Ile Leu His Pro Ser Asp Glu Leu Thr Arg Val
 20 25 30
 Thr Pro Ser Leu Asn Ser Ala Pro Thr Pro Ala Cys Gly Ser Thr Ser
 35 40 45
 His Leu Lys Ser Thr Pro Val Xaa Thr Pro Cys Thr Pro Arg Arg Leu
 50 55 60
 Ser Leu Ala Glu Ser Phe Thr Asn Thr Arg Glu Ser Thr Thr Thr Met
 65 70 75 80

540

<211> 306

<212> PRT

<213> Homo sapiens

<400> 601

Ala Cys Pro Arg Pro Thr Ala Arg Trp Gln Leu Arg Phe Trp Thr His
 1 5 10 15
 Gly Tyr Gly Tyr Arg Arg Ser Gly Arg Asp Lys Tyr Gly Pro Pro Thr
 20 25 30
 Arg Thr Glu Tyr Arg Leu Ile Val Glu Asn Leu Ser Ser Arg Cys Ser
 35 40 45
 Trp Gln Asp Leu Lys Asp Tyr Met Arg Gln Ala Gly Glu Val Thr Tyr
 50 55 60
 Ala Asp Ala His Lys Gly Arg Lys Asn Glu Gly Val Ile Glu Phe Val
 65 70 75 80
 Ser Tyr Ser Asp Met Lys Arg Ala Leu Glu Lys Leu Asp Gly Thr Glu
 85 90 95
 Val Asn Gly Arg Lys Ile Arg Leu Val Glu Asp Lys Pro Gly Ser Arg
 100 105 110
 Arg Arg Arg Ser Tyr Ser Arg Ser Arg Ser His Ser Arg Ser Arg Ser
 115 120 125
 Arg Ser Arg His Ser Arg Lys Ser Arg Ser Arg Ser Gly Ser Ser Lys
 130 135 140
 Ser Ser His Ser Lys Ser Arg Ser Arg Ser Arg Ser Gly Ser Arg Ser
 145 150 155 160
 Arg Ser Lys Ser Arg Ser Arg Ser Gln Ser Arg Ser Arg Ser Lys Lys
 165 170 175
 Glu Lys Ser Arg Ser Pro Ser Lys Asp Lys Ser Arg Ser Arg Ser His
 180 185 190
 Ser Ala Gly Lys Ser Arg Ser Lys Ser Lys Asp Gln Ala Glu Glu Lys
 195 200 205
 Ile Gln Asn Asn Asp Asn Val Gly Lys Pro Lys Ser Arg Ser Pro Ser
 210 215 220
 Arg His Lys Ser Lys Ser Lys Ser Arg Ser Arg Ser Gln Glu Arg Arg
 225 230 235 240
 Val Glu Glu Glu Lys Arg Gly Ser Val Ser Arg Gly Arg Ser Gln Glu

50 55 60
 Tyr Pro Cys Ile His Arg Pro Pro His Pro Ser Pro Ala Gln Pro Ala
 65 70 75 80
 Leu Leu Leu Gly Pro Gly Ser Leu Gln Asp Pro Arg Gly Thr Gly Ala
 85 90 95
 Glu Leu Pro Ser Gln Pro Ala Ala
 100

<210> 600

<211> 122

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (22)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 600

Thr Glu Phe Lys Lys Leu Ser Lys Gly Lys Ser Leu Leu Gly Ala Phe
 1 5 10 15

Ile Pro Arg Cys Asn Xaa Glu Gly Tyr Tyr Lys Ala Thr Gln Cys His
 20 25 30

Gly Ser Thr Gly Gln Cys Trp Cys Val Asp Lys Tyr Gly Asn Glu Leu
 35 40 45

Ala Gly Ser Arg Lys Gln Gly Ala Val Ser Cys Glu Glu Glu Gln Glu
 50 55 60

Thr Ser Gly Asp Phe Gly Ser Gly Gly Ser Val Val Leu Leu Asp Asp
 65 70 75 80

Leu Glu Tyr Glu Arg Glu Leu Gly Pro Lys Asp Lys Glu Gly Lys Leu
 85 90 95

Arg Val His Thr Arg Ala Val Thr Glu Asp Asp Glu Asp Glu Asp Asp
 100 105 110

Asp Lys Glu Asp Glu Val Gly Tyr Ile Trp
 115 120

<210> 601

Pro Arg Thr Pro Arg Pro Pro Gly Pro Pro Gly Glu Val Ile Gln Pro
 20 25 30
 Leu Pro Ile Gln Ala Ser Arg Thr Arg Arg Asn Ile Asp Ala Ser Gln
 35 40 45
 Leu Leu Asp Asp Gly Asn Gly Glu Asn Tyr Val Asp Tyr Ala Asp Gly
 50 55 60
 Met Glu Glu Ile Phe Gly Ser Leu Asn Ser Leu Lys Leu Glu Ile Glu
 65 70 75 80
 Gln Met Lys Arg Pro Leu Gly Thr Gln Gln Asn Pro Ala Arg Thr Cys
 85 90 95
 Lys Asp Leu Gln Leu Cys His Pro Asp Phe Pro Asp Gly Glu Tyr Trp
 100 105 110
 Val Asp Pro Asn Gln Gly Cys Ser Arg Asp Ser Phe Lys Val Tyr Cys
 115 120 125
 Asn Phe Thr Ala Gly Gly Ser Thr Cys Val Phe Pro Asp Lys Lys Ser
 130 135 140
 Glu Gly Pro Glu Ser Leu Leu Gly Pro Lys Lys Thr Arg Ala Pro Gly
 145 150 155 160
 Ser Val Asn Ser Ser Val Gly Asn Cys Ser Pro Met Trp Thr Pro Arg
 165 170 175
 Ala Thr Leu Trp Val Trp Tyr Arg
 180

<210> 599
 <211> 104
 <212> PRT
 <213> Homo sapiens

<400> 599
 Gly Arg Gly Ser Ala Lys Lys Arg Pro Leu Pro Leu Val Gly Ile Gly
 1 5 10 15
 Met Ser Lys Asn Thr Val Ser Ser Ala Arg Phe Arg Lys Val Asp Val
 20 25 30
 Asp Glu Tyr Asp Glu Asn Lys Phe Val Asp Glu Glu Asp Gly Gly Asp
 35 40 45
 Gly Gln Ala Gly Pro Asp Glu Gly Glu Val Asp Ser Cys Leu Arg Gln

Val Tyr Phe Met Thr Leu Asn Arg Asn Cys Ile Met Asn Trp
 500 505 510

<210> 597
 <211> 90
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (38)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (39)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 597
 Leu Ile Ser Asn Arg Asn Ser Val Phe Ser Ser Thr Val Asn Val Gly
 1 5 10 15
 Ser Lys His Ser Gly Thr Cys Arg Thr Tyr Lys Phe Val Thr Val Ile
 20 25 30
 Asp Val Ile Met Leu Xaa Xaa Asp Leu Leu Ser Glu Met Arg Thr Tyr
 35 40 45
 Pro Ser Tyr Tyr Glu Ser Cys Trp Gln Ser Ala Leu Ser Trp Gln Pro
 50 55 60
 Gln Gly Asn Gly Leu Ser Cys Arg Glu Pro Pro Gln Leu Gly Asn Lys
 65 70 75 80
 His Leu Ala Leu Phe Asp Ser Gly His Phe
 85 90

<210> 598
 <211> 184
 <212> PRT
 <213> Homo sapiens

<400> 598
 Gly Thr Arg Ala Pro Arg Val Gln Leu Ala Arg Ser Gly Gly Arg Pro
 1 5 10 15

Gly Gln Gly Lys Val Tyr Gly Leu Ile Gly Arg Arg Arg Phe Gln Gln
225 230 235 240

Met Asp Val Leu Glu Gly Leu Asn Leu Leu Ile Thr Ile Ser Gly Lys
245 250 255

Arg Asn Lys Leu Arg Val Tyr Tyr Leu Ser Trp Leu Arg Asn Lys Ile
260 265 270

Leu His Asn Asp Pro Glu Val Glu Lys Lys Gln Gly Trp Thr Thr Val
275 280 285

Gly Asp Met Glu Gly Cys Gly His Tyr Arg Xaa Val Lys Tyr Glu Arg
290 295 300

Ile Lys Phe Leu Val Ile Ala Leu Lys Ser Ser Val Glu Val Tyr Ala
305 310 315 320

Trp Ala Pro Lys Pro Tyr His Lys Phe Met Ala Phe Lys Ser Phe Ala
325 330 335

Asp Leu Pro His Arg Pro Leu Leu Val Asp Leu Thr Val Glu Glu Gly
340 345 350

Gln Arg Leu Lys Val Ile Tyr Gly Ser Ser Ala Gly Phe His Ala Val
355 360 365

Asp Val Asp Ser Gly Asn Ser Tyr Asp Ile Tyr Ile Pro Val His Ile
370 375 380

Gln Ser Gln Ile Thr Pro His Ala Ile Ile Phe Leu Pro Asn Thr Asp
385 390 395 400

Gly Met Glu Met Leu Leu Cys Tyr Glu Asp Glu Gly Val Tyr Val Asn
405 410 415

Thr Tyr Gly Arg Ile Ile Lys Asp Val Val Leu Gln Trp Gly Glu Met
420 425 430

Pro Thr Ser Val Ala Tyr Ile Cys Ser Asn Gln Ile Met Gly Trp Gly
435 440 445

Glu Lys Ala Ile Glu Ile Arg Ser Val Glu Thr Gly His Leu Asp Gly
450 455 460

Val Phe Met His Lys Arg Ala Gln Arg Leu Lys Phe Leu Cys Glu Arg
465 470 475 480

Asn Asp Lys Val Phe Phe Ala Ser Val Arg Ser Gly Gly Ser Ser Gln
485 490 495

<221> SITE

<222> (117)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (299)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 596

Tyr Ser Ser Ser Ser Glu Glu Val Glu Ser Ser Glu Asp Asp Glu Glu
 1 5 10 15

Glu Gly Glu Gly Gly Pro Ala Glu Gly Ser Arg Asp Thr Xaa Gly Gly
 20 25 30

Arg Ser Asp Gly Asp Thr Asp Ser Val Thr Pro Trp Trp Ser Thr Thr
 35 40 45

Ser Arg Arg Ser Pro Gly Pro Ser Pro His Thr Gly Arg Xaa Pro Trp
 50 55 60

Trp Ser Ser Ala Pro Leu Lys Arg Ser Gly Thr Cys Cys Met Leu Thr
 65 70 75 80

Ala Met Gly Thr Gln Thr Cys Leu Thr Trp Ser Ser Pro Ala Thr His
 85 90 95

Pro Pro Arg Thr Ala Lys Ala Lys Ala His Pro Arg Arg Met Gly Val
 100 105 110

Val Asp Tyr Gln Xaa Arg Gly Leu Val Lys Ala Pro Gly Lys Ser Ser
 115 120 125

Phe Thr Met Phe Val Asp Leu Gly Ile Tyr Gln Pro Gly Gly Ser Gly
 130 135 140

Asp Ser Ile Pro Ile Thr Ala Leu Val Gly Gly Glu Gly Thr Arg Phe
 145 150 155 160

Asp Gln Leu Gln Tyr Asp Val Arg Lys Gly Ser Val Val Asn Val Asn
 165 170 175

Pro Thr Asn Thr Arg Ala His Ser Glu Thr Pro Glu Ile Arg Lys Tyr
 180 185 190

Lys Lys Arg Phe Asn Ser Glu Ile Leu Cys Ala Ala Leu Trp Gly Val
 195 200 205

Asn Leu Leu Val Gly Thr Glu Asn Gly Leu Met Leu Leu Asp Arg Ser
 210 215 220

<210> 595
<211> 97
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 595
Ser His Phe Tyr Cys Asn Ser Phe Ser Phe Ser Arg Ala Gln Ile Asp
1 5 10 15
Gln Ala Ala Val Pro Tyr Ser Ala Gly Gln Asp Tyr Ser Ser Ile Pro
20 25 30
Ala Ser Ser Thr Gln Xaa Arg Val Trp Gly Gly Leu Phe Cys Ala Cys
35 40 45
Ser Pro His Leu Thr Leu Gly Cys His His Leu Trp Arg Leu Leu Phe
50 55 60
Gly Met Met Leu Pro Leu Ala Phe Ser Cys Tyr His Gly Leu Gly Arg
65 70 75 80
Lys His Gly Phe Gln Ile Ile Trp Glu Leu Leu Ala Met Val Pro Pro
85 90 95

Ser

<210> 596
<211> 510
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (62)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

Gln Gln Glu Leu Leu Cys Gly Gln Ile Ala Gly Val Val Arg Cys Val
 50 55 60

Ser Asp Ile Ser Asp Ser Pro Pro Thr Leu Val Arg Leu Arg Lys Leu
 65 70 75 80

Lys Phe Ala Ile Lys Val Asp Gly Asp Tyr Leu Trp Val Ser
 85 90

<210> 594

<211> 132

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (94)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 594

Thr Asn Arg Ala Gly Ile Cys Leu Leu Asp Leu Ser Cys Gly Val Pro
 1 5 10 15

Leu Leu Leu Gly Glu Ser Leu Gly Ile Lys Asn Asn His Gln Pro Gly
 20 25 30

Lys Leu Leu Cys Phe Leu Ala Asp Val Ile Pro His Trp Tyr Arg Cys
 35 40 45

Tyr Ser Val Leu Gly Gly Ser Ala Gly Lys Pro Gly Gly Thr Ser Val
 50 55 60

Ser Val Met Lys Pro Leu Thr Ala Phe Leu Thr Glu Glu Pro Ser Val
 65 70 75 80

Ile Tyr Trp Gly Arg Ser Ser Val Glu Leu Ser Ala Leu Xaa Arg Lys
 85 90 95

His Val Glu Glu Gly Arg Arg Arg Phe Pro Cys Trp Ala Cys Phe Val
 100 105 110

Glu Gly Gln Glu Gln Gln Val Met Cys Thr Cys Arg Cys Ser Thr Ser
 115 120 125

L u Cys Phe Pro
 130

Lys Glu Phe Val Ala Arg Val Arg Ala Ser Ser Arg Val Ser Gly Ser
 35 40 45
 Phe Pro Glu Asp Ser Ser Lys Glu Arg Asn Leu Val Ser Trp Glu Ser
 50 55 60
 Gln Thr Gln Pro Gln Val Gln Val Gln Asp Glu Glu Ile Thr Glu Asp
 65 70 75 80
 Asp Leu Arg Leu Ile His Glu Arg Glu Ser Ser Ile Arg Gln Leu Glu
 85 90 95
 Ala Asp Ile Met Asp Ile Asn Glu Ile Phe Lys Asp Leu Gly Met Met
 100 105 110
 Ile His Glu Gln Gly Asp Val Ile Asp Ser Ile Glu Ala Asn Val Glu
 115 120 125
 Asn Ala Glu Val His Val Gln Gln Ala Asn Gln Gln Leu Ser Arg Ala
 130 135 140
 Ala Asp Tyr Gln Arg Lys Ser Arg Lys Thr Leu Cys Ile Ile Ile Leu
 145 150 155 160
 Ile Leu Val Ile Gly Val Ala Ile Ile Ser Leu Ile Ile Trp Gly Leu
 165 170 175
 Asn His

<210> 593

<211> 94

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (14)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 593

Met Ala Thr Ser Thr Ser Thr Glu Ala Lys Ser Ala Ser Xaa Trp Asn
 1 5 10 15

Tyr Phe Phe Leu Tyr Asp Gly Ser Lys Val Lys Glu Glu Gly Asp Pro
 20 25 30

Thr Arg Ala Gly Ile Cys Tyr Phe Tyr Pro Ser Gln Thr Leu Leu Asp
 35 40 45

Gln Lys Ser Glu Pro His Ser Leu Ser Ser Glu Ala Leu Met Arg Arg
 50 55 60
 Ala Val Ser Leu Val Thr Asp Ser Thr Ser Thr Phe Leu Ser Gln Thr
 65 70 75 80
 Thr Tyr Ala Leu Ile Glu Ala Ile Thr Glu Tyr Thr Lys Ala Val Tyr
 85 90 95
 Thr Leu Thr Ser Leu Tyr Arg Gln Tyr Thr Ser Leu Leu Gly Lys Met
 100 105 110
 Asn Ser Glu Glu Glu Asp Glu Val Trp Gln Val Ile Ile Gly Ala Arg
 115 120 125
 Ala Glu Met Thr Ser Lys His Gln Glu Tyr Leu Lys Leu Glu Thr Thr
 130 135 140
 Trp Met Thr Ala Val Gly Leu Ser Glu Met Ala Ala Glu Ala Ala Tyr
 145 150 155 160
 Gln Thr Gly Ala Asp Gln Ala Ser Ile Thr Ala Arg Asn His Ile Gln
 165 170 175
 Leu Val Lys Leu Gln Val Glu Glu Val His Gln Leu Ser Arg Lys Ala
 180 185 190
 Glu Thr Lys Leu Ala Glu Ala Gln Ile Glu Glu Leu Arg Gln Lys Thr
 195 200 205
 Gln Glu Glu Gly Glu Glu Arg Ala Glu Ser Glu Gln Glu Ala Tyr Leu
 210 215 220
 Arg Glu Asp
 225

<210> 592

<211> 178

<212> PRT

<213> Homo sapiens

<400> 592

Arg Gln Arg Lys Ile Gln Lys Asp Arg Leu Val Ala Glu Phe Thr Thr
 1 5 10 15

Ser Leu Thr Asn Phe Gln Lys Val Gln Arg Gln Ala Ala Glu Arg Glu
 20 25 30

530

Val Val Leu Gln Arg Asp Trp Phe Glu Lys
 35 40

<210> 590
 <211> 35
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (15)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (21)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 590
 Thr Ala Ser Gly Ala Ala Asn Leu Ser Ile Ser Val Lys Cys Xaa Arg
 1 5 10 15

Ala Arg Thr Pro Xaa Thr Ser Leu Ala Thr Gly His Pro Glu Leu Gln
 20 25 30

Thr Trp Arg
 35

<210> 591
 <211> 227
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (1)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 591
 Xaa Ser Phe Phe Arg Tyr Arg Gln Cys Leu Cys Val Pro Val Val Ala
 1 5 10 15

Asn Phe Lys Lys Arg Cys Phe Ser Glu Leu Ile Arg Pro Trp His Lys
 20 25 30

Thr Val Thr Ile Gly Phe Gly Val Thr Leu Cys Ala Val Pro Ile Ala
 35 40 45

305 310 315 320
 Ser Gly Thr Trp Xaa Xaa Xaa Asn Leu Glu Thr Trp Glu Leu Trp Thr
 325 330 335
 Trp Lys Xaa Trp Lys Leu Glu Leu Trp Glu Leu Trp Asn Trp Lys Tyr
 340 345 350
 Trp Lys Pro Lys Pro Trp Glu Pro
 355 360

<210> 588
 <211> 88
 <212> PRT
 <213> Homo sapiens

<400> 588
 Arg Cys Leu Leu Glu Leu Gln Met His Ser Gly Leu Leu Pro Arg Pro
 1 5 10 15
 Glu Thr Phe Ser Leu Arg Lys Ala Leu Arg Thr Leu Asp Ser Leu Leu
 20 25 30
 Arg Leu Leu Ala Gln Leu His Thr Pro Ser Arg Thr Val Glu Gln Leu
 35 40 45
 Met Leu His Ala Ala Lys Leu Leu Tyr Phe Lys Gly Asn Arg Ser Ser
 50 55 60
 Thr Leu Leu His Pro Cys Phe His Thr Pro His Phe Thr Pro Leu Leu
 65 70 75 80
 Phe Ser Asp Pro Pro Leu Ala Leu
 85

<210> 589
 <211> 42
 <212> PRT
 <213> Homo sapiens

<400> 589
 Ile Ala Ser Gly Arg Ser Arg Gly Ser Lys Leu Thr Tyr Ala Cys Met
 1 5 10 15
 Arg Arg His Ser Ser Ser Ile Val Ser Pro Lys Phe Asn Ser Leu Ala
 20 25 30

35	40	45
Leu Ala Glu Gly Gly Gly Val Arg Gly Pro Arg Val Val Glu Arg His		
50	55	60
Gln Ser Ala Cys Lys Asp Ser Asp Trp Pro Phe Cys Ser Asp Glu Asp		
65	70	75
Trp Asn Tyr Lys Cys Pro Ser Gly Cys Arg Met Lys Gly Leu Ile Asp		
	85	90
Glu Val Asn Gln Asp Phe Thr Asn Arg Ile Asn Lys Leu Lys Asn Ser		
	100	105
Leu Phe Glu Tyr Gln Lys Asn Asn Lys Asp Ser His Ser Leu Thr Thr		
	115	120
Asn Ile Met Glu Ile Leu Arg Gly Asp Phe Ser Ser Ala Asn Asn Arg		
	130	135
Asp Asn Thr Tyr Asn Arg Val Ser Glu Asp Leu Arg Ser Arg Ile Glu		
145	150	155
Val Leu Lys Arg Lys Val Ile Glu Lys Val Gln His Ile Gln Leu Leu		
	165	170
Gln Lys Asn Val Arg Ala Gln Leu Val Asp Met Lys Arg Leu Glu Val		
	180	185
Asp Ile Asp Ile Lys Ile Arg Ser Cys Arg Gly Ser Cys Ser Arg Ala		
	195	200
Leu Ala Arg Glu Val Asp Leu Lys Asp Tyr Glu Asp Gln Gln Lys Gln		
	210	215
Leu Glu Gln Val Ile Ala Lys Asp Leu Leu Pro Ser Arg Asp Arg Gln		
225	230	235
His Leu Pro Leu Ile Lys Met Lys Pro Val Pro Asp Leu Val Pro Gly		
	245	250
Asn Phe Lys Ser Gln Leu Gln Lys Val Pro Pro Glu Trp Lys Ala Leu		
	260	265
Thr Asp Met Pro Gln Met Arg Met Glu Leu Glu Arg Pro Gly Gly Asn		
	275	280
Glu Ile Thr Arg Gly Gly Ser Thr Ser Tyr Gly Thr Gly Ser Glu Thr		
	290	295
Glu Ser Pro Arg Asn Pro Ser Ser Ala Gly Xaa Trp Asn Ser Gly Ser		

Arg Val Val Leu Arg Arg Trp Lys Ser Leu Lys Leu Pro Lys Lys Arg
 245 250 255

Met Ser Lys

<210> 587
 <211> 360
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (15)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (315)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (325)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (326)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (327)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (339)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 587
 Leu Asn Pro Gly Arg Pro Ala Arg Pro Val Leu Leu Arg Ser Xaa Ala
 1 5 10 15

Pro Pro Leu Glu Lys Met Phe Ser Met Arg Ile Val Cys Leu Val Leu
 20 25 30

Ser Val Val Gly Thr Ala Trp Thr Ala Asp Ser Gly Glu Gly Asp Phe

<220>

<221> SITE

<222> (199)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 586

Gln Arg Cys Phe Phe Leu Gln Thr Leu Leu Phe Leu Gln Ser Ser Ile
 1 5 10 15

Ile Ser Ala Met Ala Met Ala Ser Val Lys Leu Leu Ala Gly Val Leu
 20 25 30

Arg Lys Pro Asp Ala Trp Ile Gly Leu Trp Gly Val Leu Arg Gly Thr
 35 40 45

Pro Ser Ser Tyr Lys Leu Cys Thr Ser Trp Asn Arg Tyr Leu Tyr Phe
 50 55 60

Ser Ser Thr Lys Leu Arg Ala Pro Asn Tyr Lys Thr Leu Phe Tyr Asn
 65 70 75 80

Ile Phe Ser Leu Arg Leu Pro Gly Leu Leu Leu Ser Pro Glu Cys Ile
 85 90 95

Phe Pro Phe Ser Val Arg Leu Lys Ser Asn Ile Arg Ser Thr Lys Ser
 100 105 110

Thr Lys Lys Ser Leu Gln Lys Val Asp Glu Glu Asp Ser Asp Glu Glu
 115 120 125

Ser His His Asp Glu Met Ser Glu Gln Glu Glu Glu Leu Glu Asp Asp
 130 135 140

Pro Thr Val Val Lys Asn Tyr Lys Asp Leu Glu Lys Ala Val Gln Ser
 145 150 155 160

Phe Arg Tyr Asp Val Val Leu Lys Thr Gly Leu Asp Ile Gly Arg Asn
 165 170 175

Lys Val Glu Asp Ala Phe Tyr Lys Gly Glu Leu Arg Leu Asn Glu Glu
 180 185 190

Lys Leu Trp Lys Lys Ser Xaa Thr Val Lys Val Gly Asp Thr Leu Asp
 195 200 205

Leu Leu Ile Gly Glu Asp Lys Glu Ala Gly Thr Glu Thr Val Met Arg
 210 215 220

Ile Leu Leu Lys Lys Val Phe Glu Glu Lys Thr Glu Ser Glu Lys Tyr
 225 230 235 240

525

50	55	60
Cys Arg Phe His Ser Phe Lys Lys Val Leu Tyr Glu Met Gly Pro Glu		
65	70	75 80
Tyr Ser Ser Asn Val Glu Leu Ala Ser Phe His Ser Thr Ser Lys Gly		
	85	90 95
Tyr Met Gly Glu Cys Gly Tyr Arg Gly Gly Tyr Met Glu Val Ile Asn		
	100	105 110
Leu His Pro Glu Ile Lys Gly Gln Leu Val Lys Leu Leu Ser Val Arg		
	115	120 125
Leu Cys Pro Pro Val Ser Gly Gln Ala Ala Met Asp Ile Val Val Asn		
	130	135 140
Pro Pro Val Ala Gly Glu Glu Ser Phe Glu Gln Phe Ser Arg Glu Lys		
	145	150 155 160
Glu Ser Val Leu Gly Asn Leu Ala Lys Lys Ala Lys Leu Thr Glu Asp		
	165	170 175
Leu Phe Asn Gln Val Pro Gly Ile His Cys Asn Pro Leu Gln Gly Ala		
	180	185 190
Met Tyr Ala Phe Pro Arg Ile Phe Ile Pro Ala Lys Ala Val Glu Ala		
	195	200 205
Ala Gln Ala His Gln Met Ala Pro Asp Met Phe Tyr Cys Met Lys Leu		
	210	215 220
Leu Glu Glu Thr Gly Ile Cys Val Val Pro Gly Ser Gly Phe Gly Gln		
	225	230 235 240
Arg Glu Gly Thr Tyr His Phe Arg Met Thr Ile Leu Pro Pro Val Glu		
	245	250 255
Lys Leu Lys Thr Val Leu Gln Lys Val Lys Asp Phe His Ile Asn Phe		
	260	265 270
Leu Glu Lys Tyr Ala		
	275	

<210> 586

<211> 259

<212> PRT

<213> Homo sapiens

Ala Lys Glu Ile Ile Tyr Thr Leu Lys Glu Arg Ala Tyr Val Glu Gln
 290 295 300
 Ile Glu Lys Ala Phe Asn Tyr Ala Ser Lys Val Leu Leu Asp Phe Leu
 305 310 315 320
 Met Glu Glu Lys Glu Leu Val Ala His Leu Arg Ser Ile Lys Arg Tyr
 325 330 335
 Phe Leu Met Asp Gln Gly Asp Phe Phe Val His Phe Met Asp Leu Ala
 340 345 350
 Glu Glu Glu Leu Arg Lys Pro Val Glu Asp Ile Thr Pro Pro Arg Leu
 355 360 365
 Glu Ala Leu Leu Glu Leu Ala Leu Arg Met Ser Thr Ala Asn Thr Asp
 370 375 380
 Pro Phe Lys Asp Asp Leu Lys Ile Asp Leu Met Pro His Asp Leu Ile
 385 390 395 400
 Thr Gln Leu Leu Arg Val Leu Ala Ile Glu Thr Lys Gln Glu Lys Ala
 405 410 415
 Met Ala His Ala Xaa Pro Thr Glu Leu Ala Leu Ser Gly Leu Gly Gly
 420 425 430
 Xaa Leu Leu Ser Xaa Thr Ser Ser Ser Gly Pro Phe Arg Phe Ile His
 435 440 445
 Xaa Xaa Gly Ala Gly Ser Ala Ala Ser Gly Gln Leu
 450 455 460

<210> 585

<211> 277

<212> PRT

<213> Homo sapiens

<400> 585

Val Ile Leu Asp Gly Leu Leu Thr Trp Gly Gln Phe Lys Gln His Tyr
 1 5 10 15
 Asn Arg His Phe Gly Phe Leu Gly Asp Phe Ile Gly Gln Val Gln Ser
 20 25 30
 Arg Lys Cys Ile Glu Asp Val Ile His Phe Ala Trp Glu Glu Lys Leu
 35 40 45
 Phe Leu Leu Ala Asp Glu Val Tyr Gln Asp Asn Val Tyr Ser Pro Asp

Arg His Arg Phe Ala Asp Xaa Thr Leu Pro L u Ala Ser Gln Glu Ser
 20 25 30
 Ala Val Val Glu Asp Leu Leu Tyr Val Leu Val Gly Val Asp Gly Arg
 35 40 45
 Tyr Val Ser Ala Gln Pro Leu Ala Gly Arg Gln Ser Arg Thr Phe Leu
 50 55 60
 Val Asp Pro Asn Leu Asp Leu Ser Ile Arg Glu Leu Val His Arg Ile
 65 70 75 80
 Leu Pro Val Ala Ala Ser Tyr Ser Ala Val Thr Arg Phe Ile Glu Glu
 85 90 95
 Lys Ser Ser Phe Glu Tyr Gly Gln Val Asn His Ala Leu Xaa Ala Ala
 100 105 110
 Met Arg Thr Leu Val Lys Glu His Leu Ile Leu Val Ser Gln Leu Glu
 115 120 125
 Gln Leu His Arg Gln Gly Leu Leu Ser Leu Gln Lys Leu Trp Phe Tyr
 130 135 140
 Ile Gln Pro Ala Met Arg Thr Met Asp Ile Leu Ala Ser Leu Ala Thr
 145 150 155 160
 Ser Val Asp Lys Gly Glu Cys Leu Gly Gly Ser Thr Leu Ser Leu Leu
 165 170 175
 His Asp Arg Ser Phe Ser Tyr Thr Gly Asp Ser Gln Ala Gln Glu Leu
 180 185 190
 Cys Leu Tyr Leu Thr Lys Ala Ala Ser Ala Pro Tyr Phe Glu Val Leu
 195 200 205
 Glu Lys Trp Ile Tyr Arg Gly Ile Ile His Asp Pro Tyr Ser Glu Phe
 210 215 220
 Met Val Glu Glu His Glu Leu Arg Lys Glu Arg Ile Gln Glu Asp Tyr
 225 230 235 240
 Asn Asp Lys Tyr Trp Asp Gln Arg Tyr Thr Ile Val Gln Gln Gln Ile
 245 250 255
 Pro Ser Phe Leu Gln Lys Met Ala Asp Lys Ile Leu Ser Thr Gly Lys
 260 265 270
 Tyr Leu Asn Val Val Arg Glu Cys Gly His Asp Val Thr Cys Pro Val
 275 280 285

65 70 75 80

His Leu Gly Val Arg Asn Arg Ser Leu His Pro Gly

85 90

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<210> 584
<211> 460
<212> PRT
<213> Homo sapiens
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<220>
<221> SITE
<222> (23)
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (110)
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (421)
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (433)
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (437)
<223> xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (449)
<223> Xaa equals any of the naturally occurring L-amino acids
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<220>
<221> SITE
<222> (450)
<223> xaa equals any of the naturally occurring L-amino acids
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<400> 584
Glu Thr Cys Pro Asp Arg Gly Phe Pro Asp Trp Cys Trp His Gln His
1 5 10 15

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 582

Gly Thr Val Xaa Xaa Asn Leu Arg Lys Val Asn Thr Trp Xaa Ile Thr
1 5 10 15

Arg Ser Lys Thr Ser Ala Thr Lys Ser Phe Ile Ser Cys Phe Leu Lys
20 25 30

Ala Val Leu Cys Ile Asn Asn Lys Trp Leu Tyr Leu Thr Lys Cys Lys
35 40 45

Val Arg Ile Leu His Ile Lys Leu Phe Phe Pro
50 55

<210> 583

<211> 92

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (14)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (47)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (70)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 583

Gly Arg Val Ile Glu Glu Leu Gly Gly Ile Asp Arg Ile Xaa Ala Leu
1 5 10 15

Gln Leu His Glu Asn Arg Gln Ile Gly Gln Ser Ala Leu Asn Ile Ile
20 25 30

Glu Lys His Phe Gly Glu Lys Thr Ser Arg Ser Asn Leu Leu Xaa Ser
35 40 45

Lys Ile Lys Glu Thr Val Lys Pro Thr Arg Asn Gln Pro Ser Gly Arg
50 55 60

Gly Glu Lys Thr Thr Xaa Leu Ser Asn Glu Arg Phe Pro Gly Gln Glu

<212> PRT

<213> Homo sapiens

<400> 581

Ala Val Pro Ser Glu Phe Pro Gly Arg Pro Thr Arg Pro Gln Leu Leu
1 5 10 15

Leu Glu Phe Ser Phe Trp Asn Glu Pro Val Pro Arg Ser Gly Pro Asn
20 25 30

Ile Tyr Glu Leu Arg Ser Tyr Gln Leu Arg Pro Gly Thr Met Ile Glu
35 40 45

Trp Gly Asn Tyr Trp Ala Arg Ala Ile Arg Phe Arg Gln Asp Gly Asn
50 55 60

Glu Ala Val Gly Gly Phe Phe Ser Gln Ile Gly Gln Leu Tyr Met Val
65 70 75 80

His His Leu Trp Ala Tyr Arg Asp Leu Gln Thr Arg Glu Asp Ile Arg
85 90 95

Asn Ala Ala Trp His Lys His Gly Trp Glu Glu Leu Val Tyr Tyr Thr
100 105 110

Val Pro Leu Ile Gln Glu Met Glu Ser Arg Ile Met Ile Pro Leu Lys
115 120 125

Thr Ser Pro Leu Gln
130

<210> 582

<211> 59

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (4)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (5)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (14)

Phe Ala
210

<210> 580
<211> 154
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (146)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 580
Glu Lys Ile Ile Leu Ala Thr Gln Val Pro Cys His Val Arg Ile Gly
1 5 10 15
Gly Val Arg Leu Pro Val Val Ser Val Leu Ile His Phe Ile Thr Ser
20 25 30
Tyr Arg Ala Asn Met Asn Val Gly Val Ala His Ser Glu Val Asn Pro
35 40 45
Asn Thr Arg Val Met Asn Ser Arg Gly Met Trp Leu Thr Tyr Ala Leu
50 55 60
Gly Val Gly Leu Leu His Ile Val Leu Leu Ser Ile Pro Phe Phe Ser
65 70 75 80
Val Pro Val Ala Trp Thr Leu Thr Asn Ile Ile His Asn Leu Gly Met
85 90 95
Tyr Val Phe Leu His Ala Val Lys Gly Thr Pro Phe Glu Thr Pro Asp
100 105 110
Gln Gly Lys Ala Arg Leu Leu Thr His Trp Glu Gln Leu Asp Tyr Gly
115 120 125
Val Gln Phe Thr Ser Ser Arg Lys Phe Phe Thr Ile Ser Pro Ile Ile
130 135 140
Leu Xaa Phe Leu Ala Ser Ser Ile Arg Arg
145 150

<210> 581
<211> 133

35	40	45
Gly Thr Ile Gly Leu Trp Val Val Leu		
50	55	
<210> 579		
<211> 210		
<212> PRT		
<213> Homo sapiens		
<400> 579		
Thr Asp His Pro Gly Arg Thr Gly Arg Pro Thr Leu Pro Gly Lys Val		
1	5	10 15
Thr Glu Glu Ile Val Ser Ser Glu His Asp Glu Gly Leu Ser Phe Ser		
	20	25 30
Gly Lys Val Gln Cys Tyr Gly Arg Glu Leu Asn Gln Pro Ala Ser Ala		
	35	40 45
Ala Lys Cys Thr Gly Asp Phe Ser Pro Ser Pro Glu Lys Leu Val Lys		
	50	55 60
Ser Gly Asn Pro Leu Gln Pro Val Ser Ile Glu Asn Arg Asn Leu Asp		
	65	70 75 80
Leu Lys His Leu Val Leu Glu Ser Ser Glu Pro Pro Phe Gly Pro Arg		
	85	90 95
Asn Val Ile Glu Asn Lys Ser Leu Ser Asp Thr Leu Val Ser Thr Thr		
	100	105 110
Ala Pro Ser Gly Ile Val Asn Val Ser Val Lys Gln Gln Thr Ser Pro		
	115	120 125
Lys Ser Ser Gln Asn His Leu Phe Pro Gly Asp Leu Lys Thr Asp Glu		
	130	135 140
Gly Ile Tyr Leu Gln Val Lys Ser Leu Thr Ala Ala Ser Val Asp Gly		
	145	150 155 160
Ala Tyr Ser Thr Gln Gly Cys Met Cys Ser Val Val Pro Thr Leu Cys		
	165	170 175
Ser Ser Ser Asp Asn Ala Thr Leu Thr His Tyr Val Arg Pro Ile Asn		
	180	185 190
Ala Glu Pro Ala Phe Gln Ala Gln Asn Thr Ser Arg Gln Asn Gly Gln		
	195	200 205

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370          375          380
Ala Ala Pro Ser Arg Phe Val Leu Lys Pro Gln Arg Glu Gly Gly Gly
385          390          395          400
Asn Asn Leu Tyr Gly Glu Glu Met Val Gln Ala Leu Lys Gln Leu Lys
405          410          415
Asp Ser Glu Glu Arg Ala Ser Tyr Ile Leu Met Glu Lys Ile Glu Pro
420          425          430
Glu Pro Phe Glu Asn Cys Leu Leu Arg Pro Gly Ser Pro Ala Arg Val
435          440          445
Val Gln Cys Ile Ser Glu Leu Gly Ile Phe Gly Val Tyr Val Arg Gln
450          455          460
Glu Lys Thr Leu Val Met Asn Lys His Val Gly His Leu Leu Arg Thr
465          470          475          480
Lys Ala Ile Glu His Ala Asp Gly Gly Val Ala Ala Gly Val Ala Val
485          490          495
Leu Asp Asn Pro Tyr Pro Val
500

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<210> 578
 <211> 57
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (3)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (41)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 578
 Leu Met Xaa Lys Leu Leu Glu His Gln Asp Thr Gln Ser Gly Lys Asp
 1 5 10 15

His Arg Phe L u Val Val Ser Gly Ser Thr Arg Thr Phe Gln Ile Gln
 20 25 30

Glu Gln Arg Gln Trp Gln Arg Ser Xaa Ser Gly Gly His Gln Gly Asn

516

100	105	110
Ser Thr Ile Lys Gln Asp Asp Phe Thr Ala Arg Leu Phe Asp Ile His		
115	120	125
Lys Gln Val Leu Lys Glu Gly Ile Ala Arg Leu Xaa Xaa Phe Xaa Xaa		
130	135	140
Xaa Xaa Asp Cys Val Pro Gly Pro Glu Ser Leu Arg Leu His Val Pro		
145	150	155
Ala Gln Glu Asp Gly Ser Pro Ala Leu Lys Gln Ile Glu Ile Asn Thr		
165	170	175
Ile Ser Ala Ser Phe Gly Gly Leu Ala Ser Arg Thr Pro Ala Val His		
180	185	190
Arg His Val Leu Ser Val Leu Ser Lys Thr Lys Glu Ala Gly Lys Ile		
195	200	205
Leu Ser Asn Asn Pro Ser Lys Gly Leu Ala Leu Gly Ile Ala Lys Ala		
210	215	220
Trp Glu Leu Tyr Gly Ser Pro Asn Ala Leu Val Leu Leu Ile Ala Gln		
225	230	235
Glu Lys Glu Arg Asn Ile Phe Asp Gln Arg Ala Ile Glu Asn Glu Leu		
245	250	255
Leu Ala Arg Asn Ile His Val Ile Arg Arg Thr Phe Glu Asp Ile Ser		
260	265	270
Glu Lys Gly Ser Leu Asp Gln Asp Arg Arg Leu Phe Val Asp Gly Gln		
275	280	285
Glu Ile Ala Val Val Tyr Phe Arg Asp Gly Tyr Met Pro Arg Gln Tyr		
290	295	300
Ser Leu Gln Asn Trp Glu Ala Arg Leu Leu Leu Glu Arg Ser His Ala		
305	310	315
Ala Lys Cys Pro Asp Ile Ala Thr Gln Leu Ala Gly Thr Lys Lys Val		
325	330	335
Gln Gln Glu Leu Ser Arg Pro Gly Met Leu Glu Met Leu Leu Pro Gly		
340	345	350
Gln Pro Glu Ala Val Ala Arg Leu Arg Ala Thr Phe Ala Gly Leu Tyr		
355	360	365
Ser Leu Asp Val Gly Glu Glu Gly Asp Gln Ala Ile Ala Glu Ala Leu		

<220>

<221> SITE

<222> (140)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (141)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (143)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (144)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (145)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (146)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 577

Ala	Trp	Val	Ala	Ala	Arg	Gly	Pro	Gly	Glu	Pro	Phe	Ala	Glu	Glu	Arg
1				5					10					15	

Arg	Thr	Ser	Val	Gly	Met	Ala	Thr	Asn	Trp	Gly	Ser	Leu	Leu	Gln	Asp
			20					25					30		

Lys	Gln	Gln	Leu	Glu	Glu	Leu	Ala	Arg	Gln	Ala	Val	Asp	Arg	Ala	Leu
		35					40					45			

Ala	Glu	Gly	Val	Leu	Leu	Arg	Thr	Ser	Gln	Glu	Pro	Thr	Ser	Ser	Glu
	50					55					60				

Val	Val	Ser	Tyr	Ala	Pro	Phe	Thr	Leu	Phe	Pro	Ser	Leu	Val	Pro	Ser
65					70					75				80	

Ala	Leu	Leu	Glu	Gln	Ala	Tyr	Ala	Val	Gln	Met	Asp	Phe	Asn	Leu	Leu
				85					90					95	

Val	Asp	Ala	Val	Ser	Gln	Asn	Ala	Ala	Phe	Leu	Glu	Gln	Thr	Leu	Ser
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

514

Arg Val Val Gly Gly Glu Glu Ala Arg Pro Asn Ser Trp Pro Trp Gln
 35 40 45
 Val Ser Leu Gln Tyr Ser Ser Asn Gly Lys Trp Tyr His Thr Cys Gly
 50 55 60
 Gly Ser Leu Ile Ala Asn Ser Trp Val Leu Thr Ala Ala His Cys Ile
 65 70 75 80
 Ser Ser Ser Arg Thr Tyr Arg Val Gly Leu Gly Arg His Asn Leu Tyr
 85 90 95
 Val Ala Glu Ser Gly Ser Leu Ala Val Ser Val Ser Lys Ile Val Val
 100 105 110
 His Lys Asp Trp Asn Ser Asn Gln Ile Ser Lys Gly Asn Asp Ile Ala
 115 120 125
 Leu Leu Lys Leu Ala Asn Pro Val Ser Leu Thr Asp Lys Ile Gln Leu
 130 135 140
 Ala Cys Leu Pro Pro Ala Gly Thr Ile Leu Pro Asn Asn Tyr Pro Cys
 145 150 155 160
 Tyr Val Thr Gly Trp Gly Xaa Leu Gln Thr Asn Gly Ala Val Pro Asp
 165 170 175
 Val Leu Gln Gln Gly Arg Leu Leu Val Val Asp Tyr Ala Thr Cys Ser
 180 185 190
 Ser Ser Ala Trp Trp Gly Ser Ser Val Lys Thr Ser Met Ile Cys Ala
 195 200 205
 Gly Gly Asp Gly Xaa Ile Ser Ser Cys Asn Gly Xaa Ser Gly Gly Pro
 210 215 220
 Leu Asn Cys Gln Ala Ser Asp Gly Arg Xaa Gln Val Thr Ala Ser Ser
 225 230 235 240
 Ala Ser Gly Leu Ala Ser Ala Ala Thr Thr Thr Thr Ser Pro Pro Ser
 245 250 255
 Ser Arg Gly Ser Pro Ile Thr Ser Thr Gly Ser Ile Arg
 260 265

<210> 577

<211> 503

<212> PRT

<213> Homo sapiens

Asp Pro Ser Asn Phe Ala Asn Phe Ser Ala Tyr Pro Ser Glu Glu Asp
 115 120 125

Met Ile Glu Trp Ala Lys Arg Glu Ser Glu Arg Glu Glu Glu Gln Arg
 130 135 140

Leu Ala Arg Leu Asn Gln Gln Glu Gln Glu Asp Leu Glu Leu Ala Ile
 145 150 155 160

Ala Leu Ser Lys Ser Glu Ile Ser Glu Ala
 165 170

<210> 576

<211> 269

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (8)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (167)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (213)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (220)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (234)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 576

Leu Ser Gly His Thr Met Ile Xaa Thr Leu Leu Leu Ser Thr Leu Val
 1 5 10 15

Ala Gly Ala Leu Ser Cys Gly Asp Pro Thr Tyr Pro Pro Tyr Val Thr
 20 25 30

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                20                25                30
Asp Gln Val Ser Leu Leu Ile Ser Val Met Asp Tyr Asp Arg Val Gly
      35                40                45
His Asn Glu Ile Ile Gly Val Cys Arg Val Gly Ile Thr Ala Glu Gly
      50                55                60
Leu Gly Arg Asp His Trp Asn Glu Met Leu Ala Tyr Pro Arg Lys Pro
      65                70                75                80
Ile Ala His Trp His Ser Leu Val Glu Val Lys Lys Ser Phe Lys Glu
      85                90                95
Gly Asn Pro Arg Leu
      100

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<210> 575

<211> 170

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (26)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 575

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Leu His Thr Leu Ser Lys Val Asn Asn Glu Asp Pro Phe Arg Ser Ala
  1                5                10                15
Thr Ser Ser Ser Val Ser Asn Val Val Xaa Thr Lys Asn Val Phe Glu
      20                25                30
Glu Thr Ser Val Lys Ser Glu Asp Glu Pro Pro Ala Leu Pro Pro Lys
      35                40                45
Ile Gly Thr Pro Thr Arg Pro Cys Pro Leu Pro Pro Gly Lys Arg Ser
      50                55                60
Ile Asn Lys Leu Asp Ser Pro Asp Pro Phe Lys Leu Asn Asp Pro Phe
      65                70                75                80
Gln Pro Phe Pro Gly Asn Asp Ser Pro Lys Glu Lys Asp Pro Glu Ile
      85                90                95
Phe Cys Asp Pro Phe Thr Ser Ala Thr Thr Thr Thr Asn Lys Glu Ala
      100                105                110

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Ala Ser
145

<210> 573
<211> 139
<212> PRT
<213> Homo sapiens

<400> 573
Gly Ala Ala Glu Lys Phe Arg Glu His Arg Pro Thr Lys Leu Lys Ser
1 5 10 15
Leu Leu Arg Leu Val Asn Thr Gly Thr Ser Arg Pro Ile Ile Leu Asp
20 25 30
Pro Ala Asp Pro Thr Leu Asn Val Ala Glu Gly Tyr Arg Trp Asp Ile
35 40 45
Val Ala Gln Arg Ala Ser Gln Cys Leu Lys Gln Asp Cys Cys Tyr Asp
50 55 60
Asn Arg Glu Asn Pro Ile Ser Ser Trp Asn Val Lys Arg Ala Arg Asp
65 70 75 80
Ile His Leu Thr Val Glu Gln Arg Gly Tyr Pro Asp Phe Asn Leu Ile
85 90 95
Val Asn Pro Tyr Glu Pro Ile Arg Lys Val Lys Glu Lys Ile Arg Arg
100 105 110
Pro Gly Ala Thr Leu Ala Cys Ser Val Cys Pro Ser Arg Phe Leu Ala
115 120 125
Val Arg Gly Ser Phe Ser Ala Ala Gly Ala Pro
130 135

<210> 574
<211> 101
<212> PRT
<213> Homo sapiens

<400> 574
Arg Arg Leu Lys Lys Lys Lys Thr Thr Ile Lys Lys Asn Thr Leu Asn
1 5 10 15
Pro Val Tyr Asn Glu Ala Ile Ile Phe Asp Ile Pro Pro Glu Asn Met

<211> 146
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (1)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (114)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (141)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 572
Xaa Arg Gly Val Gly Xaa Gln Arg Cys Trp Asn Phe Val Ala Cys Leu
1 5 10 15
Pro Val Arg Ala Cys Ala Asp Met Ala Ser Asn Asp Tyr Thr Gln Gln
20 25 30
Ala Thr Gln Ser Tyr Gly Ala Tyr Pro Thr Gln Pro Gly Gln Gly Tyr
35 40 45
Ser Gln Gln Ser Ser Gln Pro Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr
50 55 60
Ser Gln Ser Thr Asp Thr Ser Gly Tyr Gly Gln Ser Ser Tyr Ser Ser
65 70 75 80
Tyr Gly Gln Ser Gln Asn Ser Glu Ser Phe Ser Ala Gly His Leu Phe
85 90 95
Leu Leu Phe Leu Asn Ile Ala Phe Leu Phe Leu Val Phe Trp Arg Arg
100 105 110
Ser Xaa Val Leu Leu Pro Arg Leu Glu Cys Ser Gly Ala Val Ser Ala
115 120 125
Ser Leu Gln His Gln Pro Thr Gly Phe Lys Arg Ile Xaa Pro Ala Ser
130 135 140

115 120 125
 Phe His Gly Gly His Ala Xaa His
 130 135

<210> 571
 <211> 79
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (13)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (64)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (71)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (79)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 571
 Trp Thr Arg Thr Glu Ile Trp Ile Leu Arg Cys Arg Xaa Gly Gly Glu
 1 5 10 15
 Gly Met Val Glu Ile Asp Ser Ser Pro Leu Leu Gly Trp Val Ile Ser
 20 25 30
 Pro Asn Asn Tyr Arg Glu Thr Val Phe Gln Leu Ser Phe His Cys Cys
 35 40 45
 Phe Gln Lys Ser Gly Glu Cys Gly Phe Arg Gln Gly Ile Asn Asp Xaa
 50 55 60
 Ile Pro Trp Tyr Tyr Ser Xaa Leu Trp Thr Phe Gly Ser Phe Xaa
 65 70 75

<210> 572

<222> (103)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (105)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (108)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (116)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (121)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (135)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 570

Ser	Cys	Gln	Tyr	Gly	Val	Gln	Ser	Asn	Lys	Asp	Gly	Ser	Glu	Lys	Leu
1				5					10					15	

Glu	Glu	Asn	Asn	Ile	Met	Thr	Gln	Glu	Ser	Arg	Ala	Cys	Ser	Ser	Val
		20						25					30		

Trp	Lys	Glu	Phe	Gly	Ser	Val	Gly	Arg	Cys	Asn	Val	His	Arg	His	Phe
	35						40					45			

Gln	Gly	Asn	Ser	Lys	Gln	Ser	Pro	Phe	Pro	Phe	Ala	Phe	Pro	Gln	Ile
	50					55				60					

Leu	Ser	Val	Tyr	Ile	Lys	Pro	Trp	Val	His	Ile	Val	Val	Val	Ile	Glu
65					70				75						80

Gly	Asn	Trp	Leu	Asn	Ser	Thr	Leu	Val	Tyr	Gly	Thr	Phe	Cys	Gly	His
			85						90					95	

Leu	Arg	Lys	Thr	Ser	Tyr	Xaa	Leu	Xaa	Gly	Gly	Xaa	Cys	Cys	Pro	Ala
			100					105						110	

Arg	Gly	Arg	Xaa	Ile	Leu	Thr	Thr	Xaa	Pro	Pro	Trp	Pro	Leu	Ser	Thr
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

Ala Arg Gly Pro Cys His Ile Trp Thr Val Leu Trp Arg Arg Gln Leu
 20 25 30

His His Ser Val Gln Leu Pro Pro Trp Trp Pro Pro Gly Gln Ile Ile
 35 40 45

Tyr Asn Trp Gln Gly Ala Gln Ser Thr Gln Asp Glu Val Ala Ala Ser
 50 55 60

Ala Ile Leu Thr Ala Gln Leu Asp Glu Glu Leu Gly Gly Thr Pro Val
 65 70 75 80

Gln Val Ser Pro Ala His Xaa Leu Ser Gly Leu Gln Pro Glu Pro Cys
 85 90 95

Pro Ser Leu His Ser Ser Val
 100

<210> 569
 <211> 72
 <212> PRT
 <213> Homo sapiens

<400> 569
 Leu Lys Val Phe His Thr Gly Glu Arg Leu Tyr Pro Leu Ile His Asp
 1 5 10 15

Val His Thr Gln Leu Ala Gly Lys Ile Thr Gly Met Leu Leu Glu Ile
 20 25 30

Asp Asn Ser Glu Leu Leu Leu Met Leu Glu Ser Pro Glu Ser Leu His
 35 40 45

Ala Lys Ile Asp Glu Ala Val Ala Val Leu Gln Ala His Gln Ala Met
 50 55 60

Glu Gln Pro Lys Ala Tyr Met His
 65 70

<210> 570
 <211> 136
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE

Leu Arg Ser Tyr Lys Tyr Tyr Thr Asp Ser Ile Val Asn Pro Asp Gly
 290 295 300
 Phe Ala Gly Phe Pro Cys Ala Ser Tyr Asn Val Phe Thr Ala Asn Lys
 305 310 315 320
 Cys Phe Pro Cys Pro Ser Gly Gly Cys Pro Gln Met Gly His Tyr Ala
 325 330 335
 Asp Arg Tyr Pro Gly Lys Thr Asn Asp Val Gly Gln Lys Phe Tyr Leu
 340 345 350
 Asp Thr Gly Asp Ala Ser Asn Phe Ala Arg Trp Arg Tyr Lys Val Ser
 355 360 365
 Val Thr Leu Ser Gly Lys Lys Val Thr Gly His Ile Leu Val Ser Leu
 370 375 380
 Phe Gly Asn Lys Gly Asn Ser Lys Gln Tyr Glu Ile Phe Lys Gly Thr
 385 390 395 400
 Leu Lys Pro Asp Ser Thr His Ser Asn Glu Phe Asp Ser Asp Val Asp
 405 410 415
 Val Gly Asp Leu Gln Met Val Lys Phe Ile Trp Tyr Asn Asn Val Ile
 420 425 430
 Asn Pro Thr Leu Pro Arg Val Gly Ala Ser Lys Ile Ile Val Glu Thr
 435 440 445
 Asn Val Gly Lys Gln Phe Asn Phe Cys Ser Pro Glu Thr Val Arg Glu
 450 455 460
 Glu Val Leu Leu Thr Leu Thr Pro Cys
 465 470

<210> 568

<211> 103

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (87)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 568

Arg Gly Thr Ala Lys Lys Gln Ser Gly Arg Ile Glu Val Pro Thr Ser
 1 5 10 15

Leu Leu Leu Gly Ala Val Ala Gly Lys Glu Val Cys Tyr Glu Arg Leu
 20 25 30

Gly Cys Phe Ser Asp Asp Ser Pro Trp Ser Gly Ile Thr Glu Arg Pro
 35 40 45

Leu His Ile Leu Pro Trp Ser Pro Lys Asp Val Asn Thr Arg Phe Leu
 50 55 60

Leu Tyr Thr Asn Glu Asn Pro Asn Asn Phe Gln Glu Val Ala Ala Asp
 65 70 75 80

Ser Ser Ser Ile Ser Gly Ser Asn Phe Lys Thr Asn Arg Lys Thr Arg
 85 90 95

Phe Ile Ile His Gly Phe Ile Asp Lys Gly Glu Glu Asn Trp Leu Ala
 100 105 110

Asn Val Cys Lys Asn Leu Phe Lys Val Glu Ser Val Asn Cys Ile Cys
 115 120 125

Val Asp Trp Lys Gly Gly Ser Arg Thr Gly Tyr Thr Gln Ala Ser Gln
 130 135 140

Asn Ile Arg Ile Val Gly Ala Glu Val Ala Tyr Phe Val Glu Phe Leu
 145 150 155 160

Gln Ser Ala Phe Gly Tyr Ser Pro Ser Asn Val His Val Ile Gly His
 165 170 175

Ser Leu Gly Ala His Ala Ala Gly Glu Ala Gly Arg Arg Thr Asn Gly
 180 185 190

Thr Ile Gly Arg Ile Thr Gly Leu Asp Pro Ala Glu Pro Cys Phe Gln
 195 200 205

Gly Thr Pro Glu Leu Val Arg Leu Asp Pro Ser Asp Ala Lys Phe Val
 210 215 220

Asp Val Ile His Thr Asp Gly Ala Pro Ile Val Pro Asn Leu Gly Phe
 225 230 235 240

Gly Met Ser Gln Val Val Gly His Leu Asp Phe Phe Pro Asn Gly Gly
 245 250 255

Val Glu Met Pro Gly Cys Lys Lys Asn Ile Leu Ser Gln Ile Val Asp
 260 265 270

Ile Asp Gly Il Trp Glu Gly Thr Arg Asp Phe Ala Ala Cys Asn His
 275 280 285

50 55 60

Lys Thr Ile Ile Ser Val Phe
65 70

<210> 566
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (36)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 566
Ser Pro Gly Leu Pro Glu Phe Gly Gln Ser Ala Ser Leu Pro Leu Leu
1 5 10 15
Pro Ala Ala Val Ala Ala Pro Phe Asp Asp Asp Asp Lys Ile Val Gly
20 25 30
Gly Tyr Xaa Xaa Glu Glu Lys Phe Cys Pro Pro Thr Arg Cys Pro Xaa
35 40 45
Asn Ser Gly
50

<210> 567
<211> 473
<212> PRT
<213> Homo sapiens

<400> 567
Ile Arg His Asp Gly Thr Ala Thr Met Leu Pro Leu Trp Thr Leu Ser
1 5 10 15

Ser Ser Gln Gln Glu Lys Glu Asp Lys Pro Ala Glu Thr Lys Lys Leu
 195 200 205

Arg Ile Ala Trp Pro Pro Pro Thr Glu Leu Gly Ser Ser Gly Ser Ala
 210 215 220

Leu Glu Glu Gly Ile Lys Met Ser Lys Pro Lys Trp Xaa Xaa Glu Asp
 225 230 235 240

Glu Ser Xaa

<210> 612
 <211> 115
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (39)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 612
 Met Arg Thr Asn Ser Phe Ala Glu Asp Leu Asp Leu Glu Gly Glu Thr
 1 5 10 15

Leu Leu Thr Pro Ile Thr His Ile Ser Gln Leu Arg Glu His His Arg
 20 25 30

Ala Thr Ile Lys Val Ile Xaa Arg Met Gln Tyr Phe Val Ala Lys Lys
 35 40 45

Lys Phe Gln Gln Ala Arg Lys Pro Tyr Asp Val Arg Asp Val Ile Glu
 50 55 60

Gln Tyr Ser Gln Gly His Leu Asn Leu Met Val Arg Ile Lys Glu Leu
 65 70 75 80

Gln Arg Arg Leu Asp Gln Ser Ile Gly Lys Pro Ser Leu Phe Ile Ser
 85 90 95

Val Ser Glu Lys Ser Lys Asp Arg Gly Thr Thr Arg Ser Ala Pro Ala
 100 105 110

Gly Thr Glu
 115

555

<210> 613
 <211> 175
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (52)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 613
 Ile Asn Met Ala Arg Met Asn Arg Pro Ala Pro Val Glu Val Thr Tyr
 1 5 10 15
 Lys Asn Met Arg Phe Leu Ile Thr His Asn Pro Thr Asn Ala Thr Leu
 20 25 30
 Asn Lys Phe Ile Glu Glu Leu Lys Lys Tyr Gly Val Thr Thr Ile Val
 35 40 45
 Arg Val Cys Xaa Ala Thr Tyr Asp Thr Thr Leu Val Glu Lys Glu Gly
 50 55 60
 Ile His Val Leu Asp Trp Pro Phe Asp Asp Gly Ala Pro Pro Ser Asn
 65 70 75 80
 Gln Ile Val Asp Asp Trp Leu Ser Leu Val Lys Ile Lys Phe Arg Glu
 85 90 95
 Glu Pro Gly Cys Cys Ile Ala Val His Cys Val Ala Gly Leu Gly Arg
 100 105 110
 Ala Pro Val Leu Val Ala Leu Ala Leu Ile Glu Gly Gly Met Lys Tyr
 115 120 125
 Glu Asp Ala Val Gln Phe Ile Arg Gln Lys Arg Arg Gly Ala Phe Asn
 130 135 140
 Ser Lys Gln Leu Leu Tyr Leu Glu Lys Tyr Arg Pro Lys Met Arg Leu
 145 150 155 160
 Arg Phe Lys Asp Ser Asn Gly His Arg Asn Asn Cys Cys Ile Gln
 165 170 175

<210> 614
 <211> 143
 <212> PRT
 <213> Homo sapiens

556

<400> 614

Thr Ser Asn Thr Ser Tyr Leu Leu Leu Asp Leu Leu Ala Gln His Ile
 1 5 10 15

Thr Ile Asn Thr Cys Lys Ile Thr Cys Ile Trp Leu Tyr Phe Tyr Leu
 20 25 30

Leu Ala Pro Arg Arg Glu Lys Lys Ile Asn Phe Glu Ser Gln Leu Gly
 35 40 45

Ile Asp Ala Leu Ile Phe Gly Tyr Phe Phe Arg Ile Phe Asn Leu Leu
 50 55 60

Trp Ser Gly Leu Arg Ser Ser Val Val Ser Gly Phe Val His Lys Arg
 65 70 75 80

Lys Ala Gln Lys Leu Asn Ala His Gly Ala Cys Ala Phe Cys Ala Pro
 85 90 95

Asn Ile Trp Met Arg Phe Phe Phe Gln Ala Tyr Ser Gln Ile Cys Val
 100 105 110

Gln Asn Phe Leu Thr Phe Leu Leu Cys Ile Ile Ile Glu Phe Ile Ala
 115 120 125

Ala Asp Phe Tyr Asn Asp Ser Cys Cys His Val Ser Leu Asn Asn
 130 135 140

<210> 615

<211> 131

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (19)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 615

Pro His His His Ser Trp Leu Cys Leu Pro Pro Pro Thr Pro Ala Val
 1 5 10 15

Pro Leu Xaa Met Glu Lys Ile Leu Ile Leu Leu Val Ala Leu Ser
 20 25 30

Val Ala Tyr Ala Ala Pro Gly Pro Arg Gly Ile Ile Ile Asn Leu Glu
 35 40 45

557

Asn Gly Glu Leu Cys Met Asn Ser Ala Gln Cys Lys Ser Asn Cys Cys
50 55 60

Gln His Ser Ser Ala Leu Gly Leu Ala Arg Cys Thr Ser Met Ala Ser
65 70 75 80

Glu Asn Ser Glu Cys Ser Val Lys Thr Leu Tyr Gly Ile Tyr Tyr Lys
85 90 95

Cys Pro Cys Glu Arg Gly Leu Thr Cys Glu Gly Asp Lys Thr Ile Val
100 105 110

Gly Ser Ile Thr Asn Thr Asn Phe Gly Ile Cys His Asp Ala Gly Arg
115 120 125

Ser Lys Gln
130

<210> 616

<211> 162

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (1)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (137)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (148)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 616

Xaa Arg Val Leu Leu Ala Gln Gln Glu Ala Arg Thr Glu Phe Leu Arg
1 5 10 15

Lys Lys Ala Arg His Gln Asn Ser Leu Pro Glu Leu Glu Ala Ala Glu
20 25 30

Ala Gly Ala Pro Gly Ser Gly Pro Val Asp Leu Phe Arg Glu Leu Leu
35 40 45

Glu Glu Gly Lys Gly Val Ile Arg Gly Asn Lys Glu Tyr Glu Glu Glu

50 55 60
 Lys Arg Gln Glu Lys Glu Arg Gln Glu Lys Ala Leu Gly Ile Leu Thr
 65 70 75 80
 Tyr Leu Gly Gln Ser Ala Ala Glu Ala Gln Thr Gln Pro Pro Trp Tyr
 85 90 95
 Gln Leu Pro Pro Gly Arg Gly Gly Pro Pro Pro Gly Pro Ala Pro Asp
 100 105 110
 Glu Lys Ile Lys Ser Arg Leu Asp Pro Leu Arg Glu Met Gln Lys His
 115 120 125
 Leu Gly Lys Lys Arg Gln His Gly Xaa Asp Glu Gly Ser Arg Ser Arg
 130 135 140
 Lys Glu Lys Xaa Gly Ser Glu Lys Gln Arg Pro Lys Glu Pro Pro Ser
 145 150 155 160
 Leu Gly

<210> 617
 <211> 288
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (78)
 <223> xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (279)
 <223> xaa equals any of the naturally occurring L-amino acids

<400> 617
 Gly Cys Gly Asp Ser Leu Ser Ser Gly Gly Gly Ala Cys Arg Ala Ala
 1 5 10 15

Ala Ala Leu Thr Val Arg Ser Pro Ala Val Pro Cys Arg Arg Glu His
 20 25 30

Ala Leu Phe His Ser Arg Asn Arg Val Pro Gln Arg Gly Gln Arg Arg
 35 40 45

Leu Arg Tyr Val Ala Tyr Asn Ile His Val Asn Gly Val Leu His Cys

559

50	55	60
Arg Val Arg Tyr Ser Gln Leu Leu Gly Leu His Glu Gln Xaa Arg Lys		
65	70	75 80
Glu Tyr Gly Ala Asn Val Leu Pro Ala Phe Pro Pro Lys Lys Leu Phe		
	85	90 95
Ser Leu Thr Pro Ala Glu Val Glu Gln Arg Arg Glu Gln Leu Glu Lys		
	100	105 110
Tyr Met Gln Ala Val Arg Gln Asp Pro Leu Leu Gly Ser Ser Glu Thr		
	115	120 125
Phe Asn Ser Phe Leu Arg Arg Ala Gln Gln Glu Thr Gln Gln Val Pro		
	130	135 140
Thr Glu Glu Val Ser Leu Glu Val Leu Leu Ser Asn Gly Gln Lys Val		
	145	150 155 160
Leu Val Asn Val Leu Thr Ser Asp Gln Thr Glu Asp Val Leu Glu Ala		
	165	170 175
Val Ala Ala Lys Leu Asp Leu Pro Asp Asp Leu Ile Gly Tyr Phe Ser		
	180	185 190
Leu Phe Leu Val Arg Glu Lys Glu Asp Gly Ala Phe Ser Phe Val Arg		
	195	200 205
Lys Leu Gln Glu Phe Glu Leu Pro Tyr Val Ser Val Thr Ser Leu Arg		
	210	215 220
Ser Gln Glu Tyr Lys Ile Val Leu Arg`Lys Ser Tyr Trp Asp Ser Ala		
	225	230 235 240
Tyr Asp Asp Asp Val Met Glu Asn Arg Val Gly Leu Asn Leu Leu Tyr		
	245	250 255
Ala Gln Thr Val Ser Asp Ile Glu Arg Gly Trp Ile Leu Val Thr Lys		
	260	265 270
Glu Gln His Arg Gln Leu Xaa Ile Ser Ala Arg Glu Lys Phe Ser Gln		
	275	280 285

<210> 618

<211> 189

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (167)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (184)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (188)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 618

Ala	Gln	Ser	Lys	Met	Ala	Ala	Leu	Arg	Ala	Leu	Cys	Gly	Phe	Arg	Gly
1				5				10						15	

Val	Ala	Ala	Gln	Val	Leu	Arg	Pro	Gly	Ala	Gly	Val	Arg	Leu	Pro	Ile
			20					25					30		

Gln	Pro	Ser	Arg	Gly	Val	Arg	Gln	Trp	Gln	Pro	Asp	Val	Glu	Trp	Ala
		35					40					45			

Gln	Gln	Phe	Gly	Gly	Ala	Val	Met	Tyr	Pro	Ser	Lys	Glu	Thr	Ala	His
	50					55					60				

Trp	Lys	Pro	Pro	Pro	Trp	Asn	Asp	Val	Asp	Pro	Pro	Lys	Asp	Thr	Ile
65					70					75				80	

Val	Lys	Asn	Ile	Thr	Leu	Asn	Phe	Gly	Pro	Gln	His	Pro	Ala	Ala	His
			85						90					95	

Gly	Val	Leu	Arg	Leu	Val	Met	Glu	Leu	Ser	Gly	Glu	Met	Val	Arg	Lys
		100						105					110		

Cys	Asp	Pro	His	Ile	Gly	Leu	Leu	His	Arg	Gly	Thr	Glu	Lys	Leu	Ile
		115					120					125			

Glu	Tyr	Lys	Thr	Tyr	Leu	Gln	Ala	Leu	Pro	Tyr	Phe	Asp	Arg	Leu	Asp
	130					135					140				

Tyr	Val	Ser	Met	Met	Cys	Asn	Glu	Gln	Ala	Tyr	Phe	Ser	Ser	Cys	Gly
145					150					155				160	

Glu	Val	Ala	Lys	His	Pro	Xaa	Ser	Ser	Ser	Gly	Thr	Trp	Ile	Arg	Val
			165						170					175	

Cys Leu Glu Lys Tyr Thr Phe Xaa Glu His Ile Xaa Leu
 180 185

<210> 619

<211> 245

<212> PRT

<213> Homo sapiens

<400> 619

Asp Tyr Arg Gly Ser His Gly Met Ala Phe Thr Phe Phe Glu Tyr Arg
 1 5 10 15

Ala Tyr Arg Ser Ile Ile Lys Asp Tyr Phe His Arg Gly Ala Lys Trp
 20 25 30

Thr Thr Ala Pro Lys Pro Thr Met Ala Asp Glu Leu Tyr Asn Gln Asp
 35 40 45

Tyr Pro Ile His Ser Val Glu Asp Arg His Lys Leu Ala Ala Gln Gly
 50 55 60

Lys Phe Val Thr Thr Glu Phe Glu Pro Cys Phe Asp Ala Ala Asp Phe
 65 70 75 80

Ile Arg Ala Gly Arg Asp Ile Phe Ala Gln Arg Ser Gln Val Thr Asn
 85 90 95

Tyr Leu Gly Ile Glu Trp Met Arg Arg His Leu Ala Pro Asp Tyr Arg
 100 105 110

Val His Ile Ile Ser Phe Lys Asp Pro Asn Pro Met His Ile Asp Ala
 115 120 125

Thr Phe Asn Ile Ile Gly Pro Gly Ile Val Leu Ser Asn Pro Asp Arg
 130 135 140

Pro Cys His Gln Ile Asp Leu Phe Lys Lys Ala Gly Trp Thr Ile Ile
 145 150 155 160

Thr Pro Pro Thr Pro Ile Ile Pro Asp Asp His Pro Leu Trp Met Ser
 165 170 175

Ser Lys Trp Leu Ser Met Asn Val Leu Met Leu Asp Glu Lys Arg Val
 180 185 190

Met Val Asp Ala Asn Glu Val Pro Ile Gln Lys Met Phe Glu Lys Leu
 195 200 205

Gly Ile Thr Thr Ile Lys Val Asn Ile Arg Asn Ala Asn Ser Leu Gly
210 215 220

Gly Gly Phe His Cys Trp Thr Cys Asp Val Arg Arg Arg Gly Thr Leu
225 230 235 240

Gln Ser Tyr Leu Asp
245

<210> 620

<211> 40

<212> PRT

<213> Homo sapiens

<400> 620

Asn Leu Glu His Leu Gly Gly Gly Arg Lys Tyr Pro Ser Tyr Leu Asp
1 5 10 15

Pro Tyr Phe Phe Leu Ser Ser Leu His Phe Gln Trp Lys Pro His Phe
20 25 30

Tyr Phe Arg Ile Arg Lys Leu Ser
35 40

<210> 621

<211> 82

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (30)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (41)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (47)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (48)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 621

Asn Ala Phe Ile Cys Thr Phe Arg Val Glu Ser Cys Phe Leu Leu Lys
1 5 10 15

Pro Phe Leu Ile Asp Ile Leu Arg Ala Ile Phe Leu Asn Xaa Pro Asp
20 25 30

Leu Leu Val Ser Glu Pro Ser Thr Xaa Ser Phe Pro Pro Gln Xaa Xaa
35 40 45

Gly Gly Asp Ser Glu Asn Gln Gly Arg Ala Gln Glu Lys Val Leu Ser
50 55 60

Glu His Gly Phe Ser Leu Val Thr Ser Asp Thr Ser Gln Glu Glu Gln
65 70 75 80

Thr Ser

<210> 622

<211> 249

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (48)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (61)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (103)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (147)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 622

Gly Glu Arg Glu Arg Glu Arg Ala Gly Phe Pro Ser Ile Pro Val Gly
1 5 10 15

564

Lys Ser Pro Met Val Glu Gln Ala Val Gln Thr Gly Ser Ala Asp Asn
 20 25 30
 Leu Asn Ala Lys Lys Leu Leu Pro Gly Lys Gly Thr Thr Gly Thr Xaa
 35 40 45
 Leu Asn Gly Arg Gln Ala Gln Pro Ser Ser Lys Thr Xaa Ser Asp Val
 50 55 60
 Val Gln Pro Ala Ala Val Gln Ala Gln Gly Gln Val Asn Asp Glu Asn
 65 70 75 80
 Arg Arg Pro Gln Arg Arg Arg Ser Gly Asn Arg Arg Thr Arg Asn Arg
 85 90 95
 Ser Arg Gly Gln Asn Arg Xaa Thr Asn Val Lys Glu Asn Thr Ile Lys
 100 105 110
 Phe Glu Gly Asp Phe Asp Phe Glu Ser Ala Asn Ala Gln Phe Asn Arg
 115 120 125
 Glu Glu Leu Asp Lys Glu Phe Lys Lys Lys Leu Asn Phe Lys Asp Asp
 130 135 140
 Lys Ala Xaa Lys Gly Glu Glu Lys Asp Leu Ala Val Val Thr Gln Ser
 145 150 155 160
 Ala Glu Ala Pro Ala Glu Glu Asp Leu Leu Gly Pro Asn Cys Tyr Tyr
 165 170 175
 Asp Lys Ser Lys Ser Phe Phe Asp Asn Ile Ser Ser Glu Leu Lys Thr
 180 185 190
 Ser Ser Arg Arg Thr Thr Trp Ala Glu Glu Arg Lys Leu Asn Thr Glu
 195 200 205
 Thr Phe Gly Val Ser Gly Arg Phe Leu Arg Gly Arg Ser Ser Arg Gly
 210 215 220
 Gly Phe Arg Gly Gly Arg Gly Asn Gly Thr Thr Arg Arg Asn Pro Thr
 225 230 235 240
 Ser His Arg Ala Gly Thr Gly Arg Val
 245

<210> 623

<211> 326

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (302)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 623

Arg	Glu	Pro	Arg	Ala	Trp	Gly	Gly	Gly	Gly	Gly	Arg	Gly	Gly	Trp	Gly
1				5					10					15	
Arg	Arg	Arg	Phe	Pro	Gly	Pro	Gly	Leu	Gln	Leu	Gly	Gly	Glu	Ala	Glu
			20					25					30		
Pro	Val	Leu	Pro	Pro	Leu	Gly	Ser	Gly	Arg	Arg	Ala	Pro	Glu	Asp	Gly
		35					40					45			
Arg	Ala	Ala	His	His	Gly	Ala	His	Leu	Leu	Gln	Gly	Asp	Glu	Ile	Trp
	50					55					60				
Asn	Ala	Leu	Thr	Asp	Asn	Tyr	Gly	Asn	Val	Met	Pro	Val	Asp	Trp	Lys
65					70					75					80
Ser	Ser	His	Thr	Arg	Thr	Leu	His	Leu	Leu	Thr	Leu	Asn	Leu	Ser	Glu
				85					90					95	
Lys	Gly	Val	Ser	Asp	Ser	Leu	Leu	Phe	Asp	Thr	Ser	Asp	Asp	Glu	Glu
		100						105					110		
Leu	Arg	Glu	Gln	Leu	Asp	Met	His	Ser	Ile	Ile	Val	Ser	Cys	Val	Asn
	115						120					125			
Asp	Glu	Pro	Leu	Phe	Thr	Ala	Asp	Gln	Val	Ile	Glu	Glu	Ile	Glu	Glu
	130					135					140				
Met	Met	Gln	Glu	Ser	Pro	Asp	Pro	Glu	Asp	Asp	Glu	Thr	Pro	Thr	Gln
145					150				155						160
Ser	Asp	Arg	Leu	Ser	Met	Leu	Ser	Gln	Glu	Ile	Gln	Thr	Leu	Lys	Arg
			165					170						175	
Ser	Ser	Thr	Gly	Ser	Tyr	Glu	Glu	Arg	Val	Lys	Arg	Leu	Ser	Val	Ser
		180						185				190			
Glu	Leu	Asn	Glu	Ile	Leu	Glu	Glu	Ile	Glu	Thr	Ala	Ile	Lys	Glu	Tyr
	195					200					205				
Ser	Glu	Glu	Leu	Val	Gln	Gln	Leu	Ala	Leu	Arg	Asp	Glu	Leu	Glu	Phe
	210					215				220					
Glu	Lys	Glu	Val	Lys	Asn	Ser	Phe	Ile	Ser	Val	Leu	Ile	Glu	Val	Gln

225 230 235 240
 Asn Lys Gln Lys Glu His Lys Glu Thr Ala Lys Lys Lys Lys Lys Leu
 245 250 255
 Lys Asn Gly Ser Ser Gln Asn Gly Lys Asn Glu Arg Ser His Met Pro
 260 265 270
 Gly Thr Tyr Leu Thr Thr Val Ile Pro Tyr Glu Lys Lys Asn Gly Pro
 275 280 285
 Pro Ser Val Glu Asp Leu Gln Ile Leu Thr Lys Ile Leu Xaa Ala Met
 290 295 300
 Lys Glu Asp Ser Glu Lys Val Pro Ser Leu Leu Thr Asp Tyr Ile Leu
 305 310 315 320
 Lys Val Leu Cys Pro Thr
 325

<210> 624
 <211> 245
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (5)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (108)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (112)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 624
 Glu Arg Ala Cys Xaa Gly Ala Leu Leu Gln His Leu Gly Ser Trp Asp
 1 5 10 15
 Gln Asp Cys Pro Asp Val Val Pro Thr Gly Leu Pro Lys Ser Gly Arg
 20 25 30
 His Pro Gln Pro Gly Leu Pro Asp Asn Pro Ala Gly His Arg Leu Lys
 35 40 45

His Tyr Ser Asp Phe Leu Glu Arg Met Pro Arg Glu Glu Ala Thr Glu
 50 55 60
 Ile Glu Gln Thr Val Gln Lys Ala Ala Gln Ala Phe Asn Ser Gly Leu
 65 70 75 80
 Leu Cys Val Ala Cys Gly Ser Tyr Arg Arg Gly Lys Ala Thr Cys Gly
 85 90 95
 Asp Val Asp Val Leu Ile Thr His Pro Asp Gly Xaa Ser His Arg Xaa
 100 105 110
 Ile Phe Ser Arg Leu Leu Asp Ser Leu Arg Gln Glu Gly Phe Leu Thr
 115 120 125
 Asp Asp Leu Val Ser Gln Glu Glu Asn Gly Gln Gln Gln Lys Tyr Leu
 130 135 140
 Gly Val Cys Arg Leu Pro Gly Pro Gly Arg Arg His Arg Arg Leu Asp
 145 150 155 160
 Ile Ile Val Val Pro Tyr Ser Glu Phe Ala Cys Ala Leu Leu Tyr Phe
 165 170 175
 Thr Gly Ser Ala His Phe Asn Arg Ser Met Arg Ala Leu Ala Lys Thr
 180 185 190
 Lys Gly Met Ser Leu Ser Glu His Ala Leu Ser Thr Ala Val Val Arg
 195 200 205
 Asn Thr His Gly Cys Lys Val Gly Pro Gly Arg Val Leu Pro Thr Pro
 210 215 220
 Thr Glu Lys Asp Val Phe Arg Leu Leu Gly Leu Pro Tyr Arg Glu Pro
 225 230 235 240
 Ala Glu Arg Asp Trp
 245

<210> 625
 <211> 150
 <212> PRT
 <213> Homo sapiens

<400> 625
 Gly Glu Arg Gly Gly Ser Pro Glu Pro Leu Arg Trp Glu Ser Pro Leu
 1 5 10 15

568

Leu Gly Pro Ser Leu Pro Ser Ser Pro Lys Leu Tyr Thr Gly Cys Ser
20 25 30

Asp Gln Pro Thr Thr His Gln Ala Ser Pro Pro Leu Cys Pro Arg Leu
35 40 45

Leu Ala Pro Ala Ala Pro Gly Ser Trp Phe Ile Leu Pro Pro Leu Ser
50 55 60

Leu Pro Ala Ser Pro Ser Val Leu Thr Trp Leu Gln Pro Ser Ser Cys
65 70 75 80

Ser Pro Trp Gly Lys Ala Ala Ser Leu Leu Leu Ser Leu His Ser Leu
85 90 95

Ala Pro Ser Leu Ser Pro Cys Leu Cys Gln Val Pro Pro Leu Ser Gln
100 105 110

Ala Ser Glu Gln Pro Trp Arg Gln Glu Gly His Val Lys Ser Phe Phe
115 120 125

Thr Val Leu Arg Arg Gln Val Glu Gly Glu Asp Ser Gly Gly Gly Ser
130 135 140

Gly Thr Ile Ser Leu Leu
145 150

<210> 626

<211> 235

<212> PRT

<213> Homo sapiens

<400> 626

Asp Gly Val Trp Val Ser Ile Arg Leu Asp Ser Thr Leu Arg Leu Tyr
1 5 10 15

His Ala His Thr Tyr Gln His Leu Gln Asp Val Asp Ile Glu Pro Tyr
20 25 30

Val Ser Lys Met Leu Gly Thr Gly Lys Leu Gly Phe Ser Phe Val Arg
35 40 45

Ile Thr Ala Leu Met Val Ser Cys Asn Arg Leu Trp Val Gly Thr Gly
50 55 60

Asn Gly Val Ile Ile Ser Ile Pro Leu Thr Glu Thr Val Ile Leu His
65 70 75 80

Gln Gly Arg Leu Leu Gly Leu Arg Ala Asn Lys Thr Ser Gly Val Pro

	85		90		95
Gly Asn Arg Pro Gly Ser Val Ile Arg Val Tyr Gly Asp Glu Asn Ser					
	100		105		110
Asp Lys Val Thr Pro Gly Thr Phe Ile Pro Tyr Cys Ser Met Ala His					
	115		120		125
Ala Gln Leu Cys Phe His Gly His Arg Asp Ala Val Lys Phe Phe Val					
	130		135		140
Ala Val Pro Gly Gln Val Ile Ser Pro Gln Ser Ser Ser Ser Gly Thr					
	145		150		155
Asp Leu Thr Gly Asp Lys Ala Gly Pro Ser Ala Gln Glu Pro Gly Ser					
	165		170		175
Gln Thr Pro Leu Lys Ser Met Leu Val Ile Ser Gly Gly Glu Gly Tyr					
	180		185		190
Ile Asp Phe Arg Met Gly Asp Glu Gly Gly Glu Ser Glu Leu Leu Gly					
	195		200		205
Glu Asp Leu Pro Leu Glu Pro Ser Val Thr Lys Ala Glu Arg Ser His					
	210		215		220
Leu Ile Val Trp Gln Val Met Tyr Gly Asn Glu					
	225		230		235

<210> 627

<211> 131

<212> PRT

<213> Homo sapiens

<400> 627

Phe Gly Thr Ser Phe Pro Ser Cys Ser Val Val Val Phe Ser Leu Leu
1 5 10 15

Leu Leu Leu Leu Leu Arg Leu Gly Glu Pro Ser Trp Gly Arg Met Val
20 25 30

Cys Glu Lys Cys Glu Lys Lys Leu Gly Thr Val Ile Thr Pro Asp Thr
35 40 45

Trp Lys Asp Gly Ala Arg Asn Thr Thr Glu Ser Gly Gly Arg Lys Leu
50 55 60

Asn Glu Asn Lys Ala Leu Thr Ser Lys Lys Ala Arg Phe Asp Pro Tyr
65 70 75 80

Gly Lys Asn Lys Phe Ser Thr Cys Arg Ile Cys Lys Ser Ser Val His
85 90 95

Gln Pro Gly Ser His Tyr Cys Gln Gly Cys Ala Tyr Lys Lys Gly Ile
100 105 110

Cys Ala Met Cys Gly Lys Lys Val Leu Asp Thr Lys Asn Tyr Lys Gln
115 120 125

Thr Ser Val
130

<210> 628

<211> 64

<212> PRT

<213> Homo sapiens

<400> 628

Leu Leu Met Val Thr Phe Leu Val Cys Ser Arg Lys Thr Cys Arg Leu
1 5 10 15

Tyr Ala Arg Tyr Val Asn Lys Asp Cys Gly Leu Lys Gly Glu Lys Leu
20 25 30

Ile Ile His Thr His Asp Lys Asn Ser Tyr Phe Leu Phe Leu Cys Leu
35 40 45

Phe Ile Gln Lys Gln Val Arg Ala Glu Lys Val Ser Ser Tyr Ser Thr
50 55 60

<210> 629

<211> 396

<212> PRT

<213> Homo sapiens

<400> 629

Val Gly Pro Ala Cys Glu Gln Thr Arg Pro Leu Arg Ala Pro Pro Ser
1 5 10 15

Ser Gln Asp Lys Ile Pro Gln Gln Asn Ser Glu Ser Ala Met Ala Lys
20 25 30

Pro Gln Val Val Val Ala Pro Val Leu Met Ser Lys Leu Ser Val Asn

571

35	40	45
Ala Pro Glu Phe Tyr Pro Ser Gly Tyr Ser Ser Ser Tyr Thr Glu Ser		
50	55	60
Tyr Glu Asp Gly Cys Glu Asp Tyr Pro Thr Leu Ser Glu Tyr Val Gln		
65	70	75
Asp Phe Leu Asn His Leu Thr Glu Gln Pro Gly Ser Phe Glu Thr Glu		
85	90	95
Ile Glu Gln Phe Ala Glu Thr Leu Asn Gly Cys Val Thr Thr Asp Asp		
100	105	110
Ala Leu Gln Glu Leu Val Glu Leu Ile Tyr Gln Gln Ala Thr Ser Ile		
115	120	125
Pro Asn Phe Ser Tyr Met Gly Ala Arg Leu Cys Asn Tyr Leu Ser His		
130	135	140
His Leu Thr Ile Ser Pro Gln Ser Gly Asn Phe Arg Gln Leu Leu Leu		
145	150	155
Gln Arg Cys Arg Thr Glu Tyr Glu Val Lys Asp Gln Ala Ala Lys Gly		
165	170	175
Asp Glu Val Thr Arg Lys Arg Phe His Ala Phe Val Leu Phe Leu Gly		
180	185	190
Glu Leu Tyr Leu Asn Leu Glu Ile Lys Gly Thr Asn Gly Gln Val Thr		
195	200	205
Arg Ala Asp Ile Leu Gln Val Gly Leu Arg Glu Leu Leu Asn Ala Leu		
210	215	220
Phe Ser Asn Pro Met Asp Asp Asn Leu Ile Cys Ala Val Lys Leu Leu		
225	230	235
Lys Leu Thr Gly Ser Val Leu Glu Asp Ala Trp Lys Glu Lys Gly Lys		
245	250	255
Met Asp Met Glu Glu Ile Ile Gln Arg Ile Glu Asn Val Val Leu Asp		
260	265	270
Ala Asn Cys Ser Arg Asp Val Lys Gln Met Leu Leu Lys Leu Val Glu		
275	280	285
Leu Arg Ser Ser Asn Trp Gly Arg Val His Ala Thr Ser Thr Tyr Arg		
290	295	300
Glu Ala Thr Pro Glu Asn Asp Pro Asn Tyr Phe Met Asn Glu Pro Thr		

305 310 315 320
 Phe Tyr Thr Ser Asp Gly Val Pro Phe Thr Ala Ala Asp Pro Asp Tyr
 325 330 335
 Gln Glu Lys Tyr Gln Glu Leu Leu Glu Arg Glu Asp Phe Phe Pro Asp
 340 345 350
 Tyr Glu Glu Asn Gly Thr Asp Leu Ser Gly Ala Gly Asp Pro Tyr Leu
 355 360 365
 Asp Asp Ile Asp Asp Glu Met Asp Pro Glu Ile Glu Glu Ala Tyr Glu
 370 375 380
 Lys Phe Cys Leu Glu Ser Glu Arg Lys Arg Lys Gln
 385 390 395

<210> 630

<211> 189

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (31)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 630

Leu Ile Leu Gly Glu Leu Glu Lys Gly Gln Ser Gln Phe Gln Ala Leu
 1 5 10 15

Cys Phe Val Thr Gln Leu Gln His Asn Glu Ile Ile Pro Ser Xaa Ala
 20 25 30

Met Ala Lys Leu Arg Gln Lys Asn Pro Arg Ala Val Arg Gln Ala Glu
 35 40 45

Glu Val Arg Gly Leu Glu His Leu His Met Asp Val Ala Val Asn Phe
 50 55 60

Ser Gln Gly Ala Leu Leu Ser Pro His Leu His Asn Val Cys Ala Glu
 65 70 75 80

Ala Val Asp Ala Ile Tyr Thr Arg Gln Glu Asp Val Arg Phe Trp Leu
 85 90 95

Glu Gln Gly Val Asp Ser Ser Val Phe Glu Ala Leu Pro Lys Ala Ser
 100 105 110

Glu Gln Ala Glu Leu Pro Arg Cys Arg Gln Val Gly Asp Arg Gly Lys
115 120 125

Pro Cys Val Cys His Tyr Gly Leu Ser Leu Ala Trp Tyr Pro Cys Met
130 135 140

Leu Lys Tyr Cys His Ser Arg Asp Arg Pro Thr Pro Tyr Lys Cys Gly
145 150 155 160

Ile Arg Ser Cys Gln Lys Ser Tyr Ser Phe Asp Phe Tyr Val Pro Gln
165 170 175

Arg Gln Leu Cys Leu Trp Asp Glu Asp Pro Tyr Pro Gly
180 185

<210> 631

<211> 32

<212> PRT

<213> Homo sapiens

<400> 631

Phe Pro Leu Ala Met Ala Pro Phe Ser Thr Ser Ala Phe His Ser Asn
1 5 10 15

Ser His Arg Arg Ile Ala Arg Thr Gln Gly Val Glu Val Ala Val Ser
20 25 30

<210> 632

<211> 144

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (17)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (31)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (86)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (87)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (89)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 632

His	Val	Pro	Ala	Arg	Gln	Ser	Leu	Val	Leu	Phe	Pro	Glu	Gln	Asp	Asp
1				5					10					15	

Xaa	Lys	Arg	Thr	Leu	Leu	Asp	Pro	Thr	Leu	Lys	Ala	Glu	Gly	Xaa	Lys
			20					25					30		

Pro	Gln	Glu	Ala	Leu	Ser	Ala	Thr	Pro	Arg	Glu	Glu	His	Lys	Gly	Leu
		35					40					45			

His	Asn	Ala	Thr	His	Pro	Leu	Leu	Ala	Lys	Cys	Tyr	Pro	Asp	Gly	Gly
	50					55					60				

Gly	Cys	Glu	Gly	Ile	Ala	Pro	Ser	His	Ile	His	Ser	Leu	Cys	Gly	Leu
65					70					75					80

Ser	Ser	Ser	Gly	Gln	Xaa	Xaa	Ala	Xaa	Ser	Gly	Leu	Ser	Ser	Leu	Cys
				85					90					95	

Ser	Val	Cys	Gly	Asp	Arg	Phe	His	Ala	Arg	Thr	Pro	Ser	Ser	Ser	Ile
			100					105					110		

Pro	His	Phe	Thr	Pro	Ser	His	Thr	Ser	Ser	Ile	Gln	Gly	Leu	Leu	Asn
		115					120					125			

Cys	Gln	Glu	Gln	Val	Leu	Glu	Phe	Pro	Ser	Pro	Ala	Glu	Ser	Phe	Ser
	130					135					140				

<210> 633

<211> 102

<212> PRT

<213> Homo sapiens

575

<220>

<221> SITE

<222> (29)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 633

Gly Cys Thr Lys Thr Ser Cys Val Thr Pro Gln Ser Cys Leu Trp Val
 1 5 10 15

Pro Ser Gln Ser Gln Gly Lys Ser Pro Gly Glu Tyr Xaa Ser Gln Gln
 20 25 30

Arg Ile Leu Thr Cys Ser Arg Ile Trp Phe Asp Phe Pro Thr Ile Trp
 35 40 45

Val Asp Ala Leu Pro Val Thr Val Ala Val Pro Ile Arg Gln Met Lys
 50 55 60

Gly Ser Ala Pro His Val Ser Trp Asn Asp Gly Pro Val Phe Arg Asp
 65 70 75 80

Leu Thr Glu Pro Thr Ser Lys Thr Ser Glu Asn Arg Lys Lys Glu Glu
 85 90 95

Asp Thr Gly Ile Asn Ser
 100

<210> 634

<211> 70

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (67)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 634

Val Gln Lys Asn Tyr Phe Glu Tyr Leu Asn Ile Cys Cys Ile Phe Phe
 1 5 10 15

Arg Ile Tyr Asn Met Ser Ser Phe Arg Met Gly Ile Tyr Val Cys Leu
 20 25 30

Pro Thr Phe Thr Val Lys Val Cys Tyr Leu Tyr Met Ser Asn Trp Leu
 35 40 45

Asn Thr Val Met Arg Ile Asn Cys Thr Glu Phe Ile Leu Lys Lys Lys
 50 55 60

Lys Lys Xaa Pro Gly Gly
65 70

<210> 635
<211> 297
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (222)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (242)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (254)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (268)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (269)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (274)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (280)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (282)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (295)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (296)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 635

Arg Thr Asp Pro Glu Glu Glu Asp Ser Glu Thr Thr Ala Ala Gly Val
 1 5 10 15

Thr Val Thr Val Ala Val Thr Cys Gly Ala Ala Gly Ser Ser Ser Ser
 20 25 30

Ala Ser Gly Pro Gly Ala Ser Pro Gly Gly Ser Glu Ala Gly Ser Gln
 35 40 45

Gly Ser Gly Glu Gly Glu Gly Val Gln Leu Thr Ala Ala Gln Glu Leu
 50 55 60

Met Ile Gln Gln Leu Val Ala Ala Gln Leu Gln Cys Asn Lys Arg Ser
 65 70 75 80

Phe Ser Asp Gln Pro Lys Val Thr Pro Trp Pro Leu Gly Ala Asp Pro
 85 90 95

Gln Ser Arg Asp Ala Arg Gln Gln Arg Phe Ala His Phe Thr Glu Leu
 100 105 110

Ala Ile Ile Ser Val Gln Glu Ile Val Asp Phe Ala Lys Gln Val Pro
 115 120 125

Gly Phe Leu Gln Leu Gly Arg Glu Asp Gln Ile Ala Leu Leu Lys Ala
 130 135 140

Ser Thr Ile Glu Ile Met Leu Leu Glu Thr Ala Arg Arg Tyr Asn His
 145 150 155 160

Glu Thr Glu Cys Ile Thr Phe Leu Lys Asp Phe Thr Tyr Ser Lys Asp
 165 170 175

Asp Phe His Arg Ala Gly Leu Gln Val Glu Phe Ile Asn Pro Ile Phe
 180 185 190

Glu Phe Ser Arg Ala Met Arg Arg Leu Gly Leu Asp Asp Ala Glu Tyr
 195 200 205

Ala Leu Leu Ile Ala Ile Asn Ile Phe Ser Ala Asp Arg Xaa Asn Val

578

210 215 220
 Gln Glu Pro Gly Arg Val Glu Ala Leu Gln Gln Pro Tyr Val Gly Gly
 225 230 235 240
 Ala Xaa Val Leu His Ala His Gln Glu Ala Ala Gly Pro Xaa Ala Phe
 245 250 255
 Pro Arg Met Leu His Glu Ala Gly Glu Pro Ala Xaa Xaa Glu Leu Leu
 260 265 270
 Cys Xaa Ser Glu Gln Val Phe Xaa Leu Xaa Gly Phe Arg Asp Lys Glu
 275 280 285
 Thr Cys Arg Leu Leu Leu Xaa Xaa Asn
 290 295

<210> 636
 <211> 113
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (8)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (87)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 636
 Val Ser Ala Ala Gly Arg Ala Xaa Arg Gln Leu Gly Ala Ala Glu Pro
 1 5 10 15
 Arg Glu Ala Glu Gly Ala Val Ala Ala Ala Thr Ala Thr Thr Thr Thr
 20 25 30
 Pro Ala Arg Val Pro Ser Leu Phe Pro Pro Gln Pro Pro Phe Ser Ser
 35 40 45
 Leu Pro Tyr Val Pro Glu Cys Gly Ser Thr Ala Ser Phe Pro Ala Ala
 50 55 60
 Arg Leu Pro Pro Asp Leu Ser Ala Arg Val Gly Thr Met Ser Leu Lys
 65 70 75 80
 Phe Gln Gly Lys Gln Cys Xaa Pro Thr Arg Met Asp Pro Lys Ser Ile

579

[illegible]

Gln

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<210> 637
<211> 71
<212> PRT
<213> Homo sapiens
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<220>  
<221> SITE  
<222> (51)  
<223> Xaa equals any of the naturally occurring L-amino acids
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<400> 637
Ser Trp Tyr Leu Phe Cys Met Asp Gly Phe Glu Phe Ser Phe Ile Ser
1 5 10 15

Asp Gln Val Leu Ser Lys Tyr Thr Val Cys His Leu His Ile Leu Ala
20 25 30

Pro Ser Phe Lys Asn Gly Leu Leu Ile Arg Asp Val Glu Arg Val Ser
35 40 45

His Ile Xaa Thr Leu Arg Asp Lys Ser Met Cys Ile Thr Asn Ile Leu
50 55 60

Cys Arg Gly Gly Val Leu Arg
65 70

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<210> 638
<211> 233
<212> PRT
<213> Homo sapiens
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<220>
<221> SITE
<222> (180)
<223> Xaa equals any of the naturally occurring L-amino acids
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<400> 638
Tyr Glu Val Leu Arg Asp Asn Thr Leu Val Thr Leu Ala Asn Ile Ser
1 5 10 15

580

Gly Gln Leu Asp Leu Ser Ala Tyr Thr Glu Ser Ile Cys Leu Pro Ile
 20 25 30
 Leu Asp Gly Leu Leu His Trp Met Val Cys Pro Ser Ala Glu Ala Gln
 35 40 45
 Asp Pro Phe Pro Thr Val Gly Pro Asn Ser Val Leu Ser Pro Gln Arg
 50 55 60
 Leu Val Leu Glu Thr Leu Cys Lys Leu Ser Ile Gln Asp Asn Asn Val
 65 70 75 80
 Asp Leu Ile Leu Ala Thr Pro Pro Phe Ser Arg Gln Glu Lys Phe Tyr
 85 90 95
 Ala Thr Leu Val Arg Tyr Val Gly Asp Arg Lys Asn Pro Val Cys Arg
 100 105 110
 Glu Met Ser Met Ala Leu Leu Ser Asn Leu Ala Gln Gly Asp Ala Leu
 115 120 125
 Ala Ala Arg Ala Ile Ala Val Gln Lys Gly Ser Ile Gly Asn Leu Ile
 130 135 140
 Ser Phe Leu Glu Asp Gly Val Thr Met Ala Gln Tyr Gln Gln Ser Gln
 145 150 155 160
 His Asn Leu Met His Met Gln Pro Pro Pro Leu Glu Pro Pro Ser Val
 165 170 175
 Asp Met Met Xaa Arg Ala Ala Lys Ala Leu Leu Ala Met Ala Arg Val
 180 185 190
 Asp Glu Asn Arg Ser Glu Phe Leu Leu His Glu Gly Arg Leu Leu Asp
 195 200 205
 Ile Ser Ile Ser Ala Val Leu Asn Ser Leu Val Ala Ser Val Ile Cys
 210 215 220
 Asp Val Leu Phe Gln Ile Gly Gln Leu
 225 230

<210> 639

<211> 106

<212> PRT

<213> Homo sapiens

<400> 639

581

Phe Ala Ala Val Gly Ala Gly Cys Val Ile Phe Leu Leu Ile Ile Ile
 1 5 10 15
 Phe Leu Thr Val Leu Leu Leu Lys Leu Arg Lys Arg His Arg Lys His
 20 25 30
 Thr Gln Gln Arg Ala Ala Ala Leu Ser Leu Ser Thr Leu Ala Ser Pro
 35 40 45
 Lys Gly Gly Ser Gly Thr Ala Gly Thr Glu Pro Ser Asp Ile Ile Ile
 50 55 60
 Pro Leu Arg Thr Thr Glu Asn Asn Tyr Cys Pro His Tyr Glu Lys Val
 65 70 75 80
 Ser Gly Asp Tyr Gly His Pro Val Tyr Ile Val Gln Glu Met Pro Pro
 85 90 95
 Gln Ser Pro Ala Asn Ile Tyr Tyr Lys Val
 100 105

<210> 640

<211> 164

<212> PRT

<213> Homo sapiens

<400> 640

Phe Met Tyr Val Phe Ser Gln Gly Asp Arg Val Val Leu Phe Ser Gln
 1 5 10 15
 Phe Thr Met Met Leu Asp Ile Leu Glu Val Leu Leu Lys His His Gln
 20 25 30
 His Arg Tyr Leu Arg Leu Asp Gly Lys Thr Gln Ile Ser Glu Arg Ile
 35 40 45
 His Leu Ile Asp Glu Phe Asn Thr Asp Met Asp Ile Phe Val Phe Leu
 50 55 60
 Leu Ser Thr Lys Ala Gly Gly Leu Gly Ile Asn Leu Thr Ser Ala Asn
 65 70 75 80
 Val Val Ile Leu His Asp Ile Asp Cys Asn Pro Tyr Asn Asp Lys Gln
 85 90 95
 Ala Glu Asp Arg Cys His Arg Val Gly Gln Thr Lys Glu Val Leu Val
 100 105 110
 Ile Lys Leu Ile Ser Gln Gly Thr Ile Glu Glu Ser Met Leu Lys Ile

582

115 120 125

Asn Gln Gln Lys Leu Lys Leu Glu Gln Asp Met Thr Thr Val Asp Glu
 130 135 140

Gly Asp Glu Gly Ser Met Pro Ala Asp Ile Ala Thr Leu Leu Lys Thr
 145 150 155 160

Ser Met Gly Leu

<210> 641
 <211> 45
 <212> PRT
 <213> Homo sapiens

<400> 641

Thr Tyr Pro Phe Thr Leu Ser Leu Cys Ala Asn Leu Ile Leu Tyr Tyr
 1 5 10 15

Ile Pro Lys Leu Tyr Ile Ala Leu Phe Leu Ser Ser Ile Leu Leu Tyr
 20 25 30

Trp Thr Ile Val Cys Ser Tyr Ala Asn Pro Thr Leu Phe
 35 40 45

<210> 642
 <211> 133
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (1)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 642

Xaa Phe Ser Gln Thr Val Ser Ala Val Cys Leu Pro Ser Ala Asp Asp
 1 5 10 15

Asp Phe Pro Ala Gly Thr Leu Cys Ala Thr Thr Gly Trp Gly Lys Thr
 20 25 30

Lys Tyr Asn Ala Asn Lys Thr Pro Asp Lys Leu Gln Gln Ala Ala Leu
 35 40 45

Pro Leu Leu Ser Asn Ala Glu Cys Lys Lys Ser Trp Gly Arg Arg Ile

583

50 55 60

Thr Asp Val Met Ile Cys Ala Gly Ala Ser Gly Val Ser Ser Cys Met
65 70 75 80

Gly Asp Ser Gly Gly Pro Leu Val Cys Gln Lys Asp Gly Ala Trp Thr
85 90 95

Leu Val Gly Ile Val Ser Trp Gly Ser Asp Thr Cys Ser Thr Ser Ser
100 105 110

Pro Gly Val Tyr Ala Arg Val Thr Lys Leu Ile Pro Trp Val Gln Lys
115 120 125

Ile Leu Ala Ala Asn
130

<210> 643
<211> 146
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (94)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (126)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (130)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (133)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

584

<222> (137)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (143)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 643

Gln Xaa Phe Gly Gln Lys Thr Leu Trp Leu Leu Ser Cys Phe Ser Leu
1 5 10 15

Val Gly Ala Ala Phe Gly Cys Gly Val Pro Ala Ile His Pro Val Leu
20 25 30

Ser Gly Leu Ser Arg Ile Val Asn Gly Glu Asp Ala Val Pro Gly Ser
35 40 45

Trp Pro Trp Gln Val Ser Leu Gln Asp Lys Thr Gly Phe His Phe Cys
50 55 60

Gly Gly Ser Leu Ile Ser Glu Asp Trp Val Val Thr Ala Ala His Cys
65 70 75 80

Gly Val Arg Thr Ser Asp Val Val Val Ala Gly Glu Phe Xaa Gln Gly
85 90 95

Ser Asp Glu Glu Asn Ile Gln Val Leu Lys Ile Ala Lys Val Phe Lys
100 105 110

Asn Pro Lys Phe Ser Ile Leu Thr Val Asn Asn Asp Ile Xaa Leu Leu
115 120 125

Lys Xaa Ala Thr Xaa Ala Pro Phe Xaa Gln Thr Val Ser Ala Xaa Cys
130 135 140

Leu Pro
145

<210> 644

<211> 349

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (110)

<223> Xaa equals any of the naturally occurring L-amino acids

585

<400> 644

Lys Val Pro Val Thr Ala Thr Ala Ala Gly Val Cys Val Trp Gln Gly
 1 5 10 15

Ala Arg Pro Gly Glu Arg Gly Val Ser Arg Cys Arg Ser Trp Gln Cys
 20 25 30

Arg Arg Trp Trp Ser Thr Pro Trp Cys Cys Ser Val Trp Trp Ile Ile
 35 40 45

Ser Thr Glu Ser Ala Arg Leu Glu Thr Arg Ser Val Leu Leu Val Cys
 50 55 60

Phe Trp Gly His Gly Lys Arg Lys Tyr Leu Met Tyr Arg Thr Val Leu
 65 70 75 80

His Ser Phe Asp Glu Asp Asp Lys Asp Asp Ser Val Trp Phe Leu Asp
 85 90 95

His Asp Tyr Leu Glu Asn Met Tyr Gly Met Phe Lys Lys Xaa Asn Ala
 100 105 110

Arg Glu Arg Ile Val Gly Trp Tyr His Thr Gly Pro Lys Leu His Lys
 115 120 125

Asn Asp Ile Ala Ile Asn Glu Leu Met Lys Arg Tyr Cys Pro Asn Ser
 130 135 140

Val Leu Val Ile Ile Asp Val Lys Pro Lys Asp Leu Gly Leu Pro Thr
 145 150 155 160

Glu Ala Tyr Ile Ser Val Glu Glu Val His Asp Asp Gly Thr Pro Thr
 165 170 175

Ser Lys Thr Phe Glu His Val Thr Ser Glu Ile Gly Ala Glu Glu Ala
 180 185 190

Glu Glu Val Gly Val Glu His Leu Leu Arg Asp Ile Lys Asp Thr Thr
 195 200 205

Val Gly Thr Leu Ser Gln Arg Ile Thr Asn Gln Val His Gly Leu Lys
 210 215 220

Gly Leu Asn Ser Lys Leu Leu Asp Ile Arg Ser Tyr Leu Glu Lys Val
 225 230 235 240

Ala Thr Gly Lys Leu Pro Ile Asn His Gln Ile Ile Tyr Gln Leu Gln
 245 250 255

Asp Val Phe Asn Leu Leu Pro Asp Val Ser Leu Gln Glu Phe Val Lys
 260 265 270

Ala Phe Tyr Leu Lys Thr Asn Asp Gln Met Val Val Val Tyr Leu Ala
275 280 285

Ser Leu Ile Arg Ser Val Val Ala Leu His Asn Leu Ile Asn Asn Lys
290 295 300

Ile Ala Asn Arg Asp Ala Glu Lys Lys Glu Gly Gln Glu Lys Glu Glu
305 310 315 320

Ser Lys Lys Asp Arg Lys Glu Asp Lys Glu Lys Asp Lys Asp Lys Glu
325 330 335

Lys Ser Asp Val Lys Lys Glu Glu Lys Lys Glu Lys Lys
340 345

<210> 645

<211> 124

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (86)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (93)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (94)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (103)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (104)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (105)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (109)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (121)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (122)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 645

Arg Cys Ser Ser Pro Ala Asp Thr Arg Arg Gly Cys Glu Val Glu Gln
1 5 10 15

Trp Asp Ser Asp Glu Pro Ile Pro Ala Lys Glu Leu Glu Arg Gly Val
20 25 30

Ala Gly Ala His Gly Leu Leu Cys Leu Leu Ser Asp His Val Asp Lys
35 40 45

Arg Ile Leu Asp Ala Ala Gly Ala Asn Leu Lys Val Ile Ser Thr Met
50 55 60

Ser Val Gly Ile Asp His Leu Ala Leu Asp Glu Ile Lys Lys Arg Gly
65 70 75 80

Ile Arg Val Gly Tyr Xaa Pro Asp Val Leu Thr Asp Xaa Xaa Ala Glu
85 90 95

Leu Ala Val Ser Leu Leu Xaa Xaa Xaa Cys Arg Arg Xaa Pro Glu Ala
100 105 110

Ser Glu Glu Val Lys Asn Gly Gly Xaa Xaa Ser Trp
115 120

<210> 646

<211> 89

<212> PRT

<213> Homo sapiens

<400> 646

Tyr Arg Glu Ser Trp Tyr Ala Cys Arg Tyr Arg Ser Gly Ile Pro Gly

588

1 5 10 15
Ser Thr His Ala Ser Ala Ala Ile Arg Leu Phe Ser Val Arg Leu Gly
20 25 30
Arg Gly Gln Gly Arg Ser Ser His Pro Cys Val Glu Gly Ser Arg Cys
35 40 45
Ala Ser Glu Gln Leu Leu Cys Ser Glu Val Leu Gly Gly Ser Asp Cys
50 55 60
Ala Ile Ile Val Ile Lys Glu Lys Thr Arg Pro Pro Ser Phe Leu Pro
65 70 75 80
Cys Trp Pro Leu Phe Ile Glu Phe Tyr
85

<210> 647

<211> 126

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (34)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (40)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (41)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (42)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (47)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (61)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (67)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (70)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (82)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (88)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (98)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (102)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (103)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (117)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <400> 647
 Ala Arg Ala Ala Pro Arg Arg Ala Glu Pro Thr Glu Pro Ala Leu Arg
 1 5 10 15

 Arg Pro Ser Ser Ala Asp Arg Pro Leu Ala Pro Gly Pro Ser Ser Ser
 20 25 30

 Pro Xaa Ala Gly Arg Ala Pro Xaa Xaa Xaa Ala Ser Pro Ser Xaa Ser

590

35 40 45
Ser Glu Ala Thr Gly Lys Pro Arg Gly Arg Asp Gly Xaa Pro Arg Arg
50 55 60
Glu Glu Xaa Asp Val Xaa Pro Glu Glu Lys Arg Leu Arg Leu Leu Leu
65 70 75 80
Glu Xaa Gly Ser Ala Gln Pro Xaa Asp Cys Glu Asp Gly Glu Asp Ala
85 90 95
Pro Xaa Pro Gly Arg Xaa Xaa Thr Gly Thr Gln Thr Gly Gly Asp Gly
100 105 110
Arg Gly Val Ser Xaa Ala Gly Ala Gly Val Arg Gly Cys Arg
115 120 125

<210> 648

<211> 121

<212> PRT

<213> Homo sapiens

<400> 648

Lys Ile Leu Asn Met Gln Lys Ser Cys Glu Glu Asn Glu Gly Lys Pro
1 5 10 15
Gln Asn Met Pro Lys Ala Glu Glu Asp Arg Pro Leu Glu Asp Val Pro
20 25 30
Gln Glu Ala Glu Gly Asn Pro Gln Pro Ser Glu Glu Gly Val Ser Arg
35 40 45
Glu Ala Glu Gly Asn Pro Arg Gly Gly Pro Asn Gln Pro Gly Gln Gly
50 55 60
Phe Lys Glu Asp Thr Pro Val Arg His Leu Asp Pro Glu Glu Met Ile
65 70 75 80
Arg Gly Val Asp Glu Leu Glu Arg Leu Arg Glu Glu Ile Arg Arg Val
85 90 95
Arg Asn Lys Phe Val Met Met His Trp Lys Gln Arg His Ser Arg Ser
100 105 110
Arg Pro Tyr Pro Val Cys Phe Arg Pro
115 120

591

<210> 649
 <211> 236
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (31)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (114)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 649
 Thr Gln Met Arg Trp Asn Cys Leu Arg Arg Arg Met Gln Cys Trp Thr
 1 5 10 15
 Arg Thr Arg Met Ser Val Trp Thr Arg Leu Pro Cys Gly Ser Xaa Thr
 20 25 30
 Glu Met Gly Phe Pro Glu Asn Arg Ala Thr Lys Ala Leu Gln Leu Asn
 35 40 45
 His Met Ser Val Pro Gln Ala Met Glu Trp Leu Ile Glu His Ala Glu
 50 55 60
 Asp Pro Thr Ile Asp Thr Pro Leu Pro Gly Gln Ala Pro Pro Glu Ala
 65 70 75 80
 Glu Gly Ala Thr Ala Ala Ala Ser Glu Ala Ala Ala Gly Ala Ser Ala
 85 90 95
 Thr Asp Glu Glu Ala Arg Asp Glu Leu Thr Glu Ile Phe Lys Lys Ile
 100 105 110
 Arg Xaa Lys Arg Glu Phe Arg Ala Asp Ala Arg Ala Val Ile Ser Leu
 115 120 125
 Met Glu Met Gly Phe Asp Glu Lys Glu Val Ile Asp Ala Leu Arg Val
 130 135 140
 Asn Asn Asn Gln Gln Asn Ala Ala Cys Glu Trp Leu Leu Gly Asp Arg
 145 150 155 160
 Lys Pro Ser Pro Glu Glu Leu Asp Lys Gly Ile Asp Pro Asp Ser Pro
 165 170 175
 Leu Phe Gln Ala Ile Leu Asp Asn Pro Val Val Gln Leu Gly Leu Thr
 180 185 190

592

Asn Pro Lys Thr Leu Leu Ala Phe Glu Asp Met Leu Glu Asn Pro Leu
 195 200 205

Asn Ser Thr Gln Trp Met Asn Asp Pro Glu Thr Gly Pro Val Met Leu
 210 215 220

Gln Ile Ser Arg Ile Phe Gln Thr Leu Asn Arg Thr
 225 230 235

<210> 650

<211> 119

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (108)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 650

Ser Ser Val Cys Met Ala Cys Thr Tyr Val Ser Asn Leu Gly Lys Lys
 1 5 10 15

Gln Arg Ser Val Ser Phe Leu Ala Ser Gly Leu Met Arg Val Ser Thr
 20 25 30

Gly Pro Glu Leu Arg Leu His His Ser Phe Val Leu Thr Gly Asp Val
 35 40 45

Gly Arg Arg Ile Cys Arg Leu Leu Val Gly Leu Phe Thr Lys Gly Asp
 50 55 60

Thr Ser Ser Lys Arg Val His Pro Phe Ser Pro Gly Pro Cys Phe Leu
 65 70 75 80

Leu Cys Asp Leu Ala Arg Val Gly Ser Ser Pro Lys Ile Asn Val Ser
 85 90 95

Pro Phe Tyr Gln Asn Gln Thr Ser Thr Gln Arg Xaa Leu Leu Ser Leu
 100 105 110

Cys Gly Lys Asp Val Pro Leu
 115

<210> 651

<211> 62

593

<212> PRT

<213> Homo sapiens

<400> 651

Asn Val Lys Gly Gln Gln Glu Pro Val Phe Leu Met Ser Ser Cys Thr
1 5 10 15

Arg His Lys Ser Lys Ala Asn Thr Ser Leu Lys Ser Arg Asn Lys Tyr
20 25 30

Phe Ser Arg Phe Leu Leu Gly His Ile Leu Thr Ala Leu Gly Ile Leu
35 40 45

Ile Trp Ser Pro Asn Thr Lys Asp Pro Phe Arg Ala Cys Tyr
50 55 60

<210> 652

<211> 64

<212> PRT

<213> Homo sapiens

<400> 652

Trp Leu Asn Asn Leu Thr Arg Leu Thr Arg Thr Val Asn Lys Leu Tyr
1 5 10 15

Val Gln Asp Tyr Asn Leu Asp Ser Leu Thr Val Glu Pro Ala Pro Leu
20 25 30

Ile Ala Ile Gln Tyr His Asn His His His His His His Pro Tyr Cys
35 40 45

Leu Ser Asp Arg Phe Leu Gly Tyr Trp Leu Asp Glu Thr Glu Tyr Met
50 55 60

<210> 653

<211> 117

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (22)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (93)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (114)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 653

Tyr Phe Glu Arg Trp Pro Pro Ala Gly Thr Gly Pro Glu Phe Pro Gly
1 5 10 15

Arg Pro Thr Arg Pro Xaa Pro Gln Ala Val Arg Ala Gly Ala Val Arg
20 25 30

Lys Leu Asp Ala Asp Glu Asp Gly Leu Pro Tyr Leu Cys Thr Gly Tyr
35 40 45

Asp Leu Tyr Val Thr Arg Glu Pro Cys Ala Met Cys Ala Met Ala Leu
50 55 60

Val His Ala Arg Ile Leu Arg Val Phe Tyr Gly Ala Pro Ser Pro Asp
65 70 75 80

Gly Ala Leu Gly Thr Arg Phe Arg Ile His Ala Arg Xaa Asp Leu Asn
85 90 95

His Arg Phe Gln Val Phe Arg Gly Val Leu Glu Glu Gln Cys Arg Trp
100 105 110

Leu Xaa Pro Asp Thr
115

<210> 654

<211> 68

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (29)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (33)

<223> Xaa equals any of the naturally occurring L-amino acids

595

<220>

<221> SITE

<222> (63)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 654

Val Asp Pro Arg Val Arg Thr His Ala Ser Val Lys Met Val Val Leu
1 5 10 15

Ile Asp Tyr Lys Arg Lys Phe Tyr Arg Ile Arg Ile Xaa Lys Thr Thr
20 25 30

Xaa Gly Ile Gly Trp Gln Cys Gln Leu Ala Leu Phe Phe Asn Ile Leu
35 40 45

Leu Phe Leu Leu Thr Leu Leu Tyr Glu Gly Thr Gly Ile Lys Xaa Thr
50 55 60

Asp Ile Pro Phe
65

<210> 655

<211> 29

<212> PRT

<213> Homo sapiens

<400> 655

Pro Val Trp Trp His Ala Pro Val Val Pro Ala Thr Arg Glu Ala Glu
1 5 10 15

Arg Gly Glu Leu Leu Glu Pro Ser Lys Gln Arg Leu Gln
20 25

<210> 656

<211> 110

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (106)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 656

Ala Arg Gly Arg Thr Ala Pro Thr Arg Gly Arg Gly Asn Gln Gly Gly
1 5 10 15

Ser Arg Glu Thr Leu Thr Glu Val Pro Trp Glu Pro Val Val Arg Arg
 20 25 30
 Ala Glu Leu Cys Gly Gln Thr Arg Gly Pro Cys Pro Pro Pro Val Lys
 35 40 45
 Pro Cys Cys Ser Arg Gly Ser His Glu Ala Glu Arg Glu Glu Cys Ser
 50 55 60
 Pro Leu Cys Thr Gln Arg Leu Pro Ser Gly Pro His Gly Leu Pro Ala
 65 70 75 80
 His Leu Gly Gly Pro Arg Asp Pro Thr Asp Pro Gln Trp His Trp Pro
 85 90 95
 Lys Met Leu Val Cys Pro Gln Gly Gln Xaa Ala Ile Leu Leu
 100 105 110

<210> 657

<211> 132

<212> PRT

<213> Homo sapiens

<400> 657

Ile Ser Trp Val Cys Leu Asn Cys Gln Ser Gln His Leu Leu Lys Ala
 1 5 10 15
 Pro Leu Ser Ser Ser Gly His Ser Gly Arg Ile Met Gly Glu Thr Glu
 20 25 30
 Gly Lys Lys Asp Glu Ala Asp Tyr Lys Arg Leu Gln Thr Phe Pro Leu
 35 40 45
 Val Arg His Ser Asp Met Pro Glu Glu Met Arg Val Glu Thr Met Glu
 50 55 60
 Leu Cys Val Thr Ala Cys Glu Lys Phe Ser Asn Asn Asn Glu Ser Ala
 65 70 75 80
 Ala Lys Met Ile Lys Glu Thr Met Asp Lys Lys Phe Gly Ser Ser Trp
 85 90 95
 His Val Val Ile Gly Glu Gly Phe Gly Phe Glu Ile Thr His Glu Val
 100 105 110
 Lys Asn Leu Leu Tyr Leu Tyr Phe Gly Gly Thr Leu Ala Val Cys Val
 115 120 125

Trp Lys Cys Ser
130

<210> 658
<211> 161
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (9)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (13)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 658
Ala Gln Pro Thr Gln Phe Pro Glu Xaa Gly Ala Val Xaa Ala Leu Gly
1 5 10 15
Pro Arg Gly Gln Gly Gly Ser Ser Leu Pro Thr Pro Pro Trp Leu Ser
20 25 30
Ser Thr Ser Trp Ala Ala Thr Ala Pro Ser Pro His Ile Ala Thr Tyr
35 40 45
Leu Glu Ala Asp Val Ala Lys Pro Ala Arg Glu Pro Thr Trp Glu Val
50 55 60
Ala Arg Thr Xaa Trp Gly Pro Arg Thr Leu Val Pro Pro Ser Ile Thr
65 70 75 80
Met Trp Val Leu Lys Thr Leu Asp Cys Leu Pro Asp Ala Pro Lys Pro
85 90 95
Asp Leu Pro Gly Trp Gly Gly Glu Asn Pro Thr Ser Pro Asp Leu His
100 105 110
His Leu His His His His His His His His His Tyr His His His
115 120 125
Pro Thr Gly Ala Arg Val Gly Lys Ile Ser Pro Leu Asp Gln Thr Ala

130 135 140
 Pro Ser Met Glu Lys Leu Glu Lys Asn Ser Gly Thr His Ile Gln Ala
 145 150 155 160

Trp

<210> 659
 <211> 171
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SITE
 <222> (45)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 659
 Pro Pro Ala Pro Pro Val His Ile Ser Ile Met Glu Gly His Tyr Tyr
 1 5 10 15
 Asp Pro Leu Gln Phe Gln Gly Pro Ile Tyr Thr His Gly Asp Ser Pro
 20 25 30
 Ala Pro Leu Pro Pro Gln Gly Met Leu Val Gln Pro Xaa Met Asn Leu
 35 40 45
 Pro His Pro Gly Leu His Pro His Gln Thr Pro Ala Pro Leu Pro Asn
 50 55 60
 Pro Gly Leu Tyr Pro Pro Pro Val Ser Met Ser Pro Gly Gln Pro Pro
 65 70 75 80
 Pro Gln Gln Leu Leu Ala Pro Thr Tyr Phe Ser Ala Pro Gly Val Met
 85 90 95
 Asn Phe Gly Asn Pro Ser Tyr Pro Tyr Ala Pro Gly Ala Leu Pro Pro
 100 105 110
 Pro Pro Pro Pro His Leu Tyr Pro Asn Thr Gln Ala Pro Ser Gln Val
 115 120 125
 Tyr Gly Gly Val Thr Tyr Tyr Asn Pro Ala Gln Gln Gln Val Gln Pro
 130 135 140
 Lys Pro Ser Pro Pro Arg Arg Thr Pro Gln Pro Val Thr Ile Lys Pro
 145 150 155 160

599

Pro Pro Pro Glu Val Val Ser Arg Gly Ser Ser
 165 170

<210> 660

<211> 215

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (85)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (188)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 660

Glu Ser Cys Leu Ser Ala Thr Gln Asp Ile Met Ala Ala His Leu Val
 1 5 10 15

Lys Arg Cys Thr Cys Leu Leu Arg Glu Ala Ala Arg Gln Ala Pro Ala
 20 25 30

Met Ala Pro Val Gly Arg Leu Arg Leu Ala Trp Val Ala His Lys Thr
 35 40 45

Leu Thr Ser Ser Ala Thr Ser Pro Ile Ser His Leu Pro Gly Ser Leu
 50 55 60

Met Glu Pro Val Glu Lys Glu Arg Ala Ser Thr Pro Tyr Ile Glu Lys
 65 70 75 80

Gln Val Asp His Xaa Ile Lys Lys Ala Thr Arg Pro Glu Glu Leu Leu
 85 90 95

Glu Leu Leu Gly Gly Ser His Asp Leu Asp Ser Asn Gln Ala Ala Met
 100 105 110

Val Leu Ile Arg Leu Ser His Leu Leu Ser Glu Lys Pro Glu Asp Lys
 115 120 125

Gly Leu Leu Ile Gln Asp Ala His Phe His Gln Leu Leu Cys Leu Leu
 130 135 140

Asn Ser Gln Ile Ala Ser Val Trp His Gly Thr Leu Ser Lys Leu Leu
 145 150 155 160

600

Gly Ser Leu Tyr Ala Leu Gly Ile Pro Lys Ala Ser Lys Glu Leu Gln
 165 170 175

Ser Val Glu Gln Glu Val Arg Trp Arg Met Arg Xaa Ala Gln Val Gln
 180 185 190

Ala Pro Gly Leu Pro Gly Arg Val Leu Cys His Pro Leu Thr Gly Ala
 195 200 205

Ala Leu Ala Gly Ala Ala Gly
 210 215

<210> 661
 <211> 272
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (261)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (262)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 661
 Asp Ala Gly Pro Leu Met Gly Thr Ser Arg Asp Gly Asp Thr Thr Arg
 1 5 10 15

Gln Arg Ile Lys Phe Ser Asp Asp Arg Val Cys Lys Ser His Leu Leu
 20 25 30

Asn Cys Cys Pro His Asp Val Leu Ser Gly Thr Arg Met Asp Leu Gly
 35 40 45

Glu Cys Leu Lys Val His Asp Leu Ala Leu Arg Ala Asp Tyr Glu Ile
 50 55 60

Ala Ser Lys Glu Gln Asp Phe Phe Phe Glu Leu Asp Ala Met Asp His
 65 70 75 80

Leu Gln Ser Phe Ile Ala Asp Cys Asp Arg Arg Thr Glu Val Ala Lys
 85 90 95

Lys Arg Leu Ala Glu Thr Gln Glu Glu Ile Ser Ala Glu Val Ala Ala
 100 105 110

601

Lys Ala Glu Arg Val His Glu Leu Asn Glu Glu Ile Gly Lys Leu Leu
 115 120 125
 Ala Lys Val Glu Gln Leu Gly Ala Glu Gly Asn Val Glu Glu Ser Gln
 130 135 140
 Lys Val Met Asp Glu Val Glu Lys Ala Arg Ala Lys Lys Arg Glu Ala
 145 150 155 160
 Glu Glu Val Tyr Arg Asn Ser Met Pro Ala Ser Ser Phe Gln Gln Gln
 165 170 175
 Lys Leu Arg Val Cys Glu Val Cys Ser Ala Tyr Leu Gly Leu His Asp
 180 185 190
 Asn Asp Arg Arg Leu Ala Asp His Phe Gly Gly Lys Leu His Leu Gly
 195 200 205
 Phe Ile Glu Ile Arg Glu Lys Leu Glu Glu Leu Lys Arg Val Val Ala
 210 215 220
 Glu Lys Gln Glu Lys Arg Asn Gln Glu Arg Leu Lys Arg Arg Glu Glu
 225 230 235 240
 Arg Glu Arg Glu Glu Arg Glu Lys Leu Arg Arg Ser Arg Ser His Ser
 245 250 255
 Lys Asn Pro Lys Xaa Xaa Arg Ser Arg Glu Arg Ser Lys Arg Arg Tyr
 260 265 270

<210> 662

<211> 152

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (14)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (89)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 662

602

Thr Glu Pro Ala Ala Gly Val Ala Val Pro Phe Ala Leu Xaa Gln His
 1 5 10 15
 Gly Arg Val Pro Ala Arg Ala Gly Pro Gly Ala Arg Leu Val Pro Ala
 20 25 30
 Arg Pro His Arg His Leu Arg Ala His Gly Glu Gln Ala Gln Ser Leu
 35 40 45
 Asp Glu Lys Gln Lys Arg Glu Glu Glu Lys Lys Ala Glu Phe Glu
 50 55 60
 Arg Gln Arg Lys Ile Arg Gln Gln Glu Ile Glu Glu Lys Leu Ile Glu
 65 70 75 80
 Glu Glu Thr Ala Arg Arg Val Glu Xaa Leu Val Ala Lys Arg Val Glu
 85 90 95
 Glu Glu Leu Glu Lys Arg Lys Asp Glu Ile Glu Arg Glu Val Leu Arg
 100 105 110
 Arg Val Glu Glu Ala Lys Arg Ile Met Glu Lys Gln Leu Leu Glu Glu
 115 120 125
 Leu Glu Arg Gln Arg Gln Ala Glu Leu Ala Ala Gln Lys Ala Arg Glu
 130 135 140
 Val Thr Leu Gly Pro Phe Gly Lys
 145 150

<210> 663

<211> 59

<212> PRT

<213> Homo sapiens

<400> 663

Pro Gln Thr Phe Asp Tyr Tyr Met Cys Ile Gly Asp Phe Asp His Pro
 1 5 10 15
 Phe Leu Ile Phe Asp Phe Cys Val Thr Tyr Cys His Leu Leu Asn Cys
 20 25 30
 Trp Pro Thr Arg Thr Gly Ser Ile Val Trp Gly Val Gly Glu Ser Leu
 35 40 45
 His Lys Glu Glu Lys Lys Leu Ser Gly Ile Leu
 50 55

603

<210> 664
 <211> 72
 <212> PRT
 <213> Homo sapiens

<400> 664
 Cys Asn Leu Leu Ile Met Pro Glu Gly Lys His Tyr Phe His Thr Leu
 1 5 10 15
 Leu Phe Leu Tyr Leu Asn Phe Leu Lys Lys Lys Ser Ser Ile Ala Leu
 20 25 30
 His Ser Phe Leu Ser Asp Ala Asp Leu Ser Phe Phe Ser Pro Phe Ile
 35 40 45
 Leu Asn Thr Met Leu His Met Asn Val Glu Ala Asp Thr Leu His Ser
 50 55 60
 Ser Val Asp Ile Thr Thr Pro Met
 65 70

<210> 665
 <211> 84
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (50)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 665
 Gly Glu Thr Arg Gly Arg Cys Met Gln Thr Ser Leu Glu Leu Trp Ser
 1 5 10 15
 Leu Leu Thr Phe Leu Pro Gln Ala Pro Leu Pro Arg Gly Pro Val Thr
 20 25 30
 Ile Leu His Arg Asp Tyr Pro Lys Thr Gln Arg Leu Ser Cys Ala Cys
 35 40 45
 Arg Xaa Ala Gln Pro Val Leu Ile Ala Ala Leu Leu Phe Asn Gln Arg
 50 55 60
 Asp Val Asn Asp Gln Val Ile Phe Ala Arg Phe Val Phe Asn Ile Phe
 65 70 75 80
 His Leu Tyr Arg

604

<210> 666
<211> 122
<212> PRT
<213> Homo sapiens

<400> 666
Ala Ser Gly Gly Gly Leu Ser Asn Ser His Leu Glu Ser Pro Phe Cys
1 5 10 15
Leu Phe Lys Ser Pro Ser Glu Gly His Ser Tyr Gln Asn Ser Gly Leu
20 25 30
Asp His Phe Gln Asn Ser Asn Ile Asp Gln Ser Phe Trp Glu Thr Phe
35 40 45
Gly Ser Ala Glu Pro Thr Lys Thr Arg Lys Ser Pro Ser Ser Asp Ser
50 55 60
Trp Thr Cys Ala Asp Thr Ser Thr Glu Arg Arg Ser Ser Asp Ser Trp
65 70 75 80
Glu Val Trp Gly Ser Ala Ser Thr Asn Arg Asn Ser Asn Ser Asp Gly
85 90 95
Gly Glu Gly Gly Glu Gly Thr Lys Lys Ala Val Pro Pro Ala Val Pro
100 105 110
Thr Asp Asp Gly Trp Asp Asn Gln Asn Trp
115 120

<210> 667
<211> 82
<212> PRT
<213> Homo sapiens

<400> 667
Arg Trp Gly Ile Cys Glu Lys Asp Val Pro Phe Ile Ile Tyr Ala Ile
1 5 10 15
Tyr Ser Arg Cys Phe Glu Arg Leu Gln Lys Arg Arg Pro Ala Ser Leu
20 25 30
Ala Asp Lys Phe Ile Ile Ile Leu Gln Lys Cys Ala Gly Cys Ala Leu
35 40 45

605

Ala Asn Cys Thr Val Leu Phe Thr Pro Ala Trp Val Thr Glu Gln Asp
 50 55 60

Ser Arg Leu Gly Gly Leu Lys Lys Lys Lys Met Leu Tyr Leu Asn Glu
 65 70 75 80

Ser Val

<210> 668
 <211> 566
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (178)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (357)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (518)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 668
 Ser Thr His Ala Ser Gly Glu Val Val Lys Pro Ala Ala Val Leu Ser
 1 5 10 15

Lys Gly Glu Ile Val Val Lys Asn Asn Pro Asn Glu Ser Val Thr Ala
 20 25 30

Asn Ala Ala Thr Asn Ser Pro Ser Cys Thr Arg Ala Asp Pro Lys Asn
 35 40 45

Val Ser Ile Pro Ser Ser Glu Ala Leu Ser Ser Asp Pro Ser Tyr Asn
 50 55 60

Lys Glu Lys His Ile Ile His Pro Thr Gln Lys Ser Lys Ala Ser Gln
 65 70 75 80

Gly Ser Asp Leu Glu Gln Asn Glu Ala Ser Arg Lys Asn Lys Lys Lys
 85 90 95

Lys Glu Lys Ser Thr Ser Lys Tyr Glu Val Leu Thr Val Gln Glu Pro

606

100	105	110
Pro Arg Ile Glu Asp Ala Glu Glu Phe Pro Asn Leu Ala Val Ala Ser		
115	120	125
Glu Arg Arg Asp Arg Ile Glu Thr Pro Lys Phe Gln Ser Lys Gln Gln		
130	135	140
Pro Gln Asp Asn Phe Lys Asn Asn Val Lys Lys Ser Gln Leu Pro Val		
145	150	155
Gln Leu Asp Leu Gly Gly Met Leu Thr Ala Leu Glu Lys Lys Gln His		
165	170	175
Ser Xaa His Ala Lys Gln Ser Ser Lys Pro Val Val Val Ser Val Gly		
180	185	190
Ala Val Pro Val Leu Ser Lys Glu Cys Ala Ser Gly Glu Arg Gly Arg		
195	200	205
Arg Met Ser Gln Met Lys Thr Pro His Asn Pro Leu Asp Ser Ser Ala		
210	215	220
Pro Leu Met Lys Lys Gly Lys Gln Arg Glu Ile Pro Lys Ala Lys Lys		
225	230	235
Pro Thr Ser Leu Lys Lys Ile Ile Leu Lys Glu Arg Gln Glu Arg Lys		
245	250	255
Gln Arg Leu Gln Glu Asn Ala Val Ser Pro Ala Phe Thr Ser Asp Asp		
260	265	270
Thr Gln Asp Gly Glu Ser Gly Gly Asp Asp Gln Phe Pro Glu Gln Ala		
275	280	285
Glu Leu Ser Gly Pro Glu Gly Met Asp Glu Leu Ile Ser Thr Pro Ser		
290	295	300
Val Glu Asp Lys Ser Glu Glu Pro Pro Gly Thr Glu Leu Gln Arg Asp		
305	310	315
Thr Glu Ala Ser His Leu Ala Pro Asn His Thr Thr Phe Pro Lys Ile		
325	330	335
His Ser Arg Arg Phe Arg Asp Tyr Cys Ser Gln Met Leu Ser Lys Glu		
340	345	350
Val Asp Ala Cys Xaa Thr Asp Leu Leu Lys Glu Leu Val Arg Phe Gln		
355	360	365
Asp Arg Met Tyr Gln Lys Asp Pro Val Lys Ala Lys Thr Lys Arg Arg		

607

370 375 380
 Leu Val Leu Gly Leu Arg Glu Val Leu Lys His Leu Lys Leu Lys Lys
 385 390 395 400
 Leu Lys Cys Val Ile Ile Ser Pro Asn Cys Glu Lys Ile Gln Ser Lys
 405 410 415
 Gly Gly Leu Asp Asp Thr Leu His Thr Ile Ile Asp Tyr Ala Cys Glu
 420 425 430
 Gln Asn Ile Pro Phe Val Phe Ala Leu Asn Arg Lys Ala Leu Gly Arg
 435 440 445
 Ser Leu Asn Lys Ala Val Pro Val Ser Val Val Gly Ile Phe Ser Tyr
 450 455 460
 Asp Gly Ala Gln Asp Gln Phe His Lys Met Val Glu Leu Thr Val Ala
 465 470 475 480
 Ala Arg Gln Ala Tyr Lys Thr Met Leu Glu Asn Val Gln Gln Glu Leu
 485 490 495
 Val Gly Glu Pro Arg Pro Gln Ala Pro Pro Ser Leu Pro Thr Gln Gly
 500 505 510
 Pro Ser Cys Pro Ala Xaa Asp Gly Pro Pro Ala Leu Lys Glu Lys Glu
 515 520 525
 Glu Pro His Tyr Ile Glu Ile Trp Lys Lys His Leu Glu Ala Tyr Ser
 530 535 540
 Gly Cys Thr Leu Glu Leu Glu Glu Ser Leu Glu Ala Ser Thr Ser Gln
 545 550 555 560
 Met Met Asn Leu Asn Leu
 565

<210> 669

<211> 114

<212> PRT

<213> Homo sapiens

<400> 669

Gly Phe Trp Asp Ser Gly Leu Cys Gly Leu Cys Leu Leu Ala Gly Asn
 1 5 10 15

Gly Leu Ser Leu Ser Arg Pro Ala Pro Pro Arg Leu Cys Leu Ser Glu
 20 25 30

Ala Pro Glu Pro Ser Ser Asp Leu Gln Asn Val Ala Ser Asp Gly Gly
 35 40 45

Leu Gly Trp Glu Met Gly Arg Ala Tyr Ile Val Phe Cys Ser Leu Lys
 50 55 60

Thr Leu Ile Ala Pro Ile Phe Gln Arg Met Val Leu Cys Glu Gln His
 65 70 75 80

Ala Ser Lys Arg Glu Ile Gly Gly Arg Gly Ser Arg Gly Gly Trp Glu
 85 90 95

Lys Ser Gly Ser Phe Leu Pro Leu Thr Ala Leu Thr Phe Cys Glu Arg
 100 105 110

Glu Ala

<210> 670
 <211> 154
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (146)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (153)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 670
 Asn Gln Arg Leu Leu Asn Asn Leu Pro Ser Phe Pro Ile Phe Cys Gly
 1 5 10 15

Pro Thr Thr Leu Gly Asp Pro Arg Leu Gly Gly Ala Pro Pro Gly Leu
 20 25 30

Ser Arg Ser Phe Arg Leu Pro Pro Leu Pro Ala Ala Met Ala Glu Leu
 35 40 45

Gly Leu Asn Glu His His Gln Asn Glu Val Ile Asn Tyr Met Arg Phe
 50 55 60

Ala Arg Ser Lys Arg Gly Leu Arg Leu Lys Thr Val Asp Ser Cys Phe
 65 70 75 80

Gln Asp Leu Lys Glu Ser Arg Leu Val Glu Asp Thr Phe Thr Ile Asp
85 90 95

Glu Val Ser Glu Val Leu Asn Gly Leu Gln Ala Val Val His Ser Glu
100 105 110

Val Glu Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn Val Leu Leu Leu
115 120 125

Arg His Cys Leu His Lys Leu Arg Ser Gly Ile Leu Ser Tyr Arg Gln
130 135 140

Thr Xaa Leu Asn Leu Lys Thr Glu Xaa Tyr
145 150

<210> 671
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (60)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (70)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (72)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (80)

610

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 671

Cys Arg Gln Glu Arg Ala Val Ala Pro Ala Arg Arg Ala Met Glu Arg
1 5 10 15

Ile Pro Ser Ala Gln Pro Pro Pro Ala Cys Leu Pro Lys Ala Pro Gly
20 25 30

Leu Glu His Gly Asp Leu Pro Gly Met Tyr Pro Ala His Met Tyr Gln
35 40 45

Val Tyr Lys Ser Arg Arg Gly Ile Lys Arg Xaa Xaa Asp Ser Lys Glu
50 55 60

Thr Tyr Lys Leu Pro Xaa Arg Xaa Ile Glu Lys Arg Asp Xaa Thr Xaa
65 70 75 80

<210> 672

<211> 224

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (220)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 672

Glu Pro Ala Glu Gly Pro Ser Ser Cys Asp Pro Ile Cys Pro Ala Gly
1 5 10 15

Leu Lys Ala Leu Ser Leu Cys Val Ala Leu Pro Pro Gly Leu Ala Val
20 25 30

Ser Val Leu Lys Ala Ile Phe Gln Glu Val His Val Gln Ser Leu Pro
35 40 45

Gln Val Asp Arg His Thr Val Tyr Asn Ile Ile Thr Asn Phe Met Arg
50 55 60

Thr Arg Glu Glu Glu Leu Lys Ser Leu Gly Ala Asp Phe Thr Phe Gly
65 70 75 80

Phe Ile Gln Val Met Asp Gly Glu Lys Asp Pro Arg Asn Leu Leu Val
85 90 95

611

Ala	Phe	Arg	Ile	Val	His	Asp	Leu	Ile	Ser	Arg	Asp	Tyr	Ser	Leu	Gly
			100					105					110		
Pro	Phe	Val	Glu	Glu	Leu	Phe	Glu	Val	Thr	Ser	Cys	Tyr	Phe	Pro	Ile
		115					120					125			
Asp	Phe	Thr	Pro	Pro	Pro	Asn	Asp	Pro	His	Gly	Ile	Gln	Arg	Glu	Asp
		130					135				140				
Leu	Ile	Leu	Ser	Leu	Arg	Ala	Val	Leu	Ala	Ser	Thr	Pro	Arg	Phe	Ala
145					150					155					160
Glu	Phe	Leu	Leu	Pro	Leu	Leu	Ile	Glu	Lys	Val	Asp	Ser	Glu	Val	Leu
				165					170					175	
Ser	Ala	Lys	Leu	Asp	Ser	Leu	Gln	Thr	Leu	Asn	Ala	Cys	Cys	Ala	Val
			180					185					190		
Tyr	Gly	Gln	Lys	Glu	Leu	Lys	Asp	Phe	Leu	Pro	Ser	Leu	Trp	Ala	Ser
		195					200					205			
Ile	Arg	Arg	Glu	Val	Phe	Gln	Thr	Ala	Val	Ser	Xaa	Trp	Arg	Gln	Arg
	210					215					220				

<210> 673

<211> 498

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (1)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (405)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (414)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (445)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 673

Xaa Leu Ser Asp Gly Arg Leu Arg Val Gly Tyr Val Ser Ser Asp Phe
 1 5 10 15

Gly Asn His Pro Thr Ser His Leu Met Gln Ser Ile Pro Gly Met His
 20 25 30

Asn Pro Asp Lys Phe Glu Val Phe Cys Tyr Ala Leu Ser Pro Asp Asp
 35 40 45

Gly Thr Asn Phe Arg Val Lys Val Met Ala Glu Ala Asn His Phe Ile
 50 55 60

Asp Leu Ser Gln Ile Pro Cys Asn Gly Lys Ala Ala Asp Arg Ile His
 65 70 75 80

Gln Asp Gly Ile His Ile Leu Val Asn Met Asn Gly Tyr Thr Lys Gly
 85 90 95

Ala Arg Asn Glu Leu Phe Ala Leu Arg Pro Ala Pro Ile Gln Ala Met
 100 105 110

Trp Leu Gly Tyr Pro Gly Thr Ser Gly Ala Leu Phe Met Asp Tyr Ile
 115 120 125

Ile Thr Asp Gln Glu Thr Ser Pro Ala Glu Val Ala Glu Gln Tyr Ser
 130 135 140

Glu Lys Leu Ala Tyr Met Pro His Thr Phe Phe Ile Gly Asp His Ala
 145 150 155 160

Asn Met Phe Pro His Leu Lys Lys Lys Ala Val Ile Asp Phe Lys Ser
 165 170 175

Asn Gly His Ile Tyr Asp Asn Arg Ile Val Leu Asn Gly Ile Asp Leu
 180 185 190

Lys Ala Phe Leu Asp Ser Leu Pro Asp Val Lys Ile Val Lys Met Lys
 195 200 205

Cys Pro Asp Gly Gly Asp Asn Ala Asp Ser Ser Asn Thr Ala Leu Asn
 210 215 220

Met Pro Val Ile Pro Met Asn Thr Ile Ala Glu Ala Val Ile Glu Met
 225 230 235 240

Ile Asn Arg Gly Gln Ile Gln Ile Thr Ile Asn Gly Phe Ser Ile Ser

613

245	250	255
Asn Gly Leu Ala Thr Thr Gln Ile Asn Asn Lys Ala Ala Thr Gly Glu		
260	265	270
Glu Val Pro Arg Thr Ile Ile Val Thr Thr Arg Ser Gln Tyr Gly Leu		
275	280	285
Pro Glu Asp Ala Ile Val Tyr Cys Asn Phe Asn Gln Leu Tyr Lys Ile		
290	295	300
Asp Pro Ser Thr Leu Gln Met Trp Ala Asn Ile Leu Lys Arg Val Pro		
305	310	315
Asn Ser Val Leu Trp Leu Leu Arg Phe Pro Ala Val Gly Glu Pro Asn		
325	330	335
Ile Gln Gln Tyr Ala Gln Asn Met Gly Leu Pro Gln Asn Arg Ile Ile		
340	345	350
Phe Ser Pro Val Ala Pro Lys Glu Glu His Val Arg Arg Gly Gln Leu		
355	360	365
Ala Asp Val Cys Leu Asp Thr Pro Leu Cys Asn Gly His Thr Thr Gly		
370	375	380
Met Asp Val Leu Trp Ala Gly Thr Pro Met Val Thr Met Pro Gly Arg		
385	390	395
Asp Ser Cys Phe Xaa Glu Leu Gln His Pro Ser Ser Leu Xaa Leu Gly		
405	410	415
Cys Leu Glu Leu Ile Ala Lys Asn Arg Gln Glu Tyr Glu Asp Ile Ala		
420	425	430
Val Lys Leu Gly Thr Asp Leu Glu Tyr Leu Lys Lys Xaa Arg Gly Lys		
435	440	445
Val Trp Lys Gln Arg Ile Ser Ser Pro Leu Phe Asn Thr Lys Gln Tyr		
450	455	460
Thr Met Glu Leu Glu Arg Leu Tyr Leu Gln Met Trp Glu His Tyr Ala		
465	470	475
Ala Gly Asn Lys Pro Asp His Met Ile Lys Pro Val Glu Val Thr Glu		
485	490	495
Ser Ala		

614

<210> 674
 <211> 146
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (15)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 674
 Arg Asp Pro Ala Gly Ser Pro Ser Ala Ala Gly Gly Leu Ala Xaa Val
 1 5 10 15
 Ser Leu Ala Leu Gly Ser Gly Ser Arg Gly Arg Asp His Ser Gly Ser
 20 25 30
 Gly Val Gly Thr Ala Met Ala Gly Ala Leu Val Arg Lys Ala Ala Asp
 35 40 45
 Tyr Val Arg Ser Lys Asp Phe Arg Asp Tyr Leu Met Ser Thr His Phe
 50 55 60
 Trp Gly Pro Val Ala Asn Trp Gly Leu Pro Ile Ala Ala Ile Asn Asp
 65 70 75 80
 Met Lys Lys Ser Pro Glu Ile Ile Ser Gly Arg Met Thr Phe Ala Leu
 85 90 95
 Cys Cys Tyr Ser Leu Thr Phe Met Arg Phe Ala Tyr Lys Val Gln Pro
 100 105 110
 Arg Asn Trp Leu Leu Phe Ala Cys His Ala Thr Asn Glu Val Ala Gln
 115 120 125
 Leu Ile Gln Gly Gly Arg Leu Ile Lys His Glu Met Thr Lys Thr Ala
 130 135 140
 Ser Ala
 145

<210> 675
 <211> 107
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE

615

<222> (27)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 675

Tyr Ser Phe Asp Leu Ile Leu Cys Leu Arg Glu Cys Ser Gly Gln Val
 1 5 10 15

Leu Cys Val Val Gly Trp Gly Gly Arg Val Xaa Ser Phe Pro His Pro
 20 25 30

Cys Val Val Val Leu Leu Thr Val Ala Pro Trp Asp Trp Leu Pro Phe
 35 40 45

Leu Leu Gly Glu Pro Gly Glu Pro Ala His Leu Val Ser Arg Val Cys
 50 55 60

Ala Trp Arg Ser Ala Pro Pro Ala Leu Met Ala Leu Cys His Arg Gln
 65 70 75 80

Arg Pro Gly Gly Ala Val Cys Ala Gln Pro Lys His Phe Thr Phe Phe
 85 90 95

Thr Leu Phe Phe Phe Phe Asn Gln Leu Ile Val
 100 105

<210> 676

<211> 90

<212> PRT

<213> Homo sapiens

<400> 676

Asn Thr Ser His Ile Ser Tyr Leu Thr Arg Leu Ser Trp Ser Cys Arg
 1 5 10 15

Phe His Cys Pro Pro Lys Thr Arg Thr His Thr Tyr Pro Tyr Thr Lys
 20 25 30

Gly Lys Thr Ile Leu Lys Cys Cys Phe Ser Gly Gly Ser Leu Ser Gly
 35 40 45

Cys Cys Leu Thr Val Trp Glu Pro Val Leu Cys Arg Gly Asp Arg Pro
 50 55 60

Asp Leu His Tyr Leu Thr Thr Leu Ala Leu Gly Ala Asn Cys Pro Thr
 65 70 75 80

Val Lys Cys Leu Gly Gly Cys Pro Ile Pro
 85 90

<210> 677

<211> 362

<212> PRT

<213> Homo sapiens

<400> 677

Ile Ile Met Ala Pro Leu Gly Thr Thr Val Leu Leu Trp Ser Leu Leu
1 5 10 15

Arg Ser Ser Pro Gly Val Glu Arg Val Cys Phe Arg Ala Arg Ile Gln
20 25 30

Pro Trp His Gly Gly Leu Leu Gln Pro Leu Pro Cys Ser Phe Glu Met
35 40 45

Gly Leu Pro Arg Arg Arg Phe Ser Ser Glu Ala Ala Glu Ser Gly Ser
50 55 60

Pro Glu Thr Lys Lys Pro Thr Phe Met Asp Glu Glu Val Gln Ser Ile
65 70 75 80

Leu Thr Lys Met Thr Gly Leu Asn Leu Gln Lys Thr Phe Lys Pro Ala
85 90 95

Ile Gln Glu Leu Lys Pro Pro Thr Tyr Lys Leu Met Thr Gln Ala Gln
100 105 110

Leu Glu Glu Ala Thr Arg Gln Ala Val Glu Ala Ala Lys Val Arg Leu
115 120 125

Lys Met Pro Pro Val Leu Glu Glu Arg Val Pro Ile Asn Asp Val Leu
130 135 140

Ala Glu Asp Lys Ile Leu Glu Gly Thr Glu Thr Thr Lys Tyr Val Phe
145 150 155 160

Thr Asp Ile Ser Tyr Ser Ile Pro His Arg Glu Arg Phe Ile Val Val
165 170 175

Arg Glu Pro Ser Gly Thr Leu Arg Lys Ala Ser Trp Glu Glu Arg Asp
180 185 190

Arg Met Ile Gln Val Tyr Phe Pro Lys Glu Gly Arg Lys Ile Leu Thr
195 200 205

Pro Ile Ile Phe Lys Glu Glu Asn Leu Arg Thr Met Tyr Ser Gln Asp
210 215 220

Arg His Val Asp Val Leu Asn Leu Cys Phe Ala Gln Phe Glu Pro Asp

617

[illegible]

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<210> 678
<211> 53
<212> PRT
<213> Homo sapiens
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<400> 678
Leu Gln Val Asp Glu Arg Arg Met Phe Met Phe Leu Tyr Gly Leu Asn
 1             5             10             15

Lys Ser Val Ile Thr Met Leu Thr Cys Ser Val Ile Lys Cys Thr Asn
      20             25             30

Gly Ser Leu Cys His Ser Phe Ile Phe Ser Gly Tyr Gln Asp Ser Gln
      35             40             45

Ile Lys Leu Leu Met
      50

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<210> 679
<211> 395
<212> PRT
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<213> Homo sapiens

<220>

<221> SITE

<222> (1)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (370)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (377)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 679

Xaa Cys Arg His Ser Ser Leu Ile Phe Pro Pro Val Ser Ala Ser Ser
1 5 10 15

Ser Ser Phe Gln Trp Phe Gln Ser Thr Val Ser Lys Glu Asp Ala Met
20 25 30

Pro Glu Ala Leu Lys Ser Leu Ile Phe Pro Asn Phe Glu Pro Leu His
35 40 45

Lys Phe His Thr Asn Phe Leu Lys Glu Ile Glu Gln Arg Leu Ala Leu
50 55 60

Trp Glu Gly Arg Ser Asn Ala Gln Ile Arg Asp Tyr Gln Arg Ile Gly
65 70 75 80

Asp Val Met Leu Lys Asn Ile Gln Gly Met Lys His Leu Ala Ala His
85 90 95

Leu Trp Lys His Ser Glu Ala Leu Glu Ala Leu Glu Asn Gly Ile Lys
100 105 110

Ser Ser Arg Arg Leu Glu Asn Phe Cys Arg Asp Phe Glu Leu Gln Lys
115 120 125

Val Cys Tyr Leu Pro Leu Asn Thr Phe Leu Leu Arg Pro Leu His Arg
130 135 140

Leu Met His Tyr Lys Gln Val Leu Glu Arg Leu Cys Lys His His Pro
145 150 155 160

Pro Ser His Ala Asp Phe Arg Asp Cys Arg Ala Ala Leu Ala Glu Ile
165 170 175

619

Thr Glu Met Val Ala Gln Leu His Gly Thr Met Ile Lys Met Glu Asn
 180 185 190
 Phe Gln Lys Leu His Glu Leu Lys Lys Asp Leu Ile Gly Ile Asp Asn
 195 200 205
 Leu Val Val Pro Gly Arg Glu Phe Ile Arg Leu Gly Ser Leu Ser Lys
 210 215 220
 Leu Ser Gly Lys Gly Leu Gln Gln Arg Met Phe Phe Leu Phe Asn Asp
 225 230 235 240
 Val Leu Leu Tyr Thr Ser Arg Gly Leu Thr Ala Ser Asn Gln Phe Lys
 245 250 255
 Val His Gly Gln Leu Pro Leu Tyr Gly Met Thr Ile Glu Glu Ser Glu
 260 265 270
 Asp Glu Trp Gly Val Pro His Cys Leu Thr Leu Arg Gly Gln Arg Gln
 275 280 285
 Ser Ile Ile Val Ala Ala Ser Ser Arg Ser Glu Met Glu Lys Trp Val
 290 295 300
 Glu Asp Ile Gln Met Ala Ile Asp Leu Ala Glu Lys Ser Ser Ser Pro
 305 310 315 320
 Ala Pro Glu Phe Leu Ala Ser Ser Pro Pro Asp Asn Lys Ser Pro Asp
 325 330 335
 Glu Ala Thr Ala Ala Asp Gln Glu Ser Glu Asp Asp Leu Ser Ala Ser
 340 345 350
 Pro His Arg Trp Ser Ala Arg Pro Arg Thr Ala Ala Thr Gln Trp Cys
 355 360 365
 Thr Xaa Ala Gly Thr Ala Thr Pro Xaa Ser Pro Trp Trp Thr Ser Ala
 370 375 380
 Ser Gln Trp Arg Ile Ser Cys Leu Glu Thr Cys
 385 390 395

<210> 680

<211> 156

<212> PRT

<213> Homo sapiens

<400> 680

Ala Arg Gly Lys Met Glu Asp Glu Glu Val Ala Glu Ser Trp Glu Glu

620

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      1             5             10             15
Ala Ala Asp Ser Gly Glu Ile Asp Arg Arg Leu Glu Lys Lys Leu Lys
      20             25             30
Ile Thr Gln Lys Glu Ser Arg Lys Ser Lys Ser Pro Pro Lys Val Pro
      35             40             45
Ile Val Ile Gln Asp Asp Ser Leu Pro Ala Gly Pro Pro Pro Gln Ile
      50             55             60
Arg Ile Leu Lys Arg Pro Thr Ser Asn Gly Val Val Ser Ser Pro Asn
      65             70             75             80
Ser Thr Ser Arg Pro Thr Leu Pro Val Lys Ser Leu Ala Gln Arg Glu
      85             90             95
Ala Glu Tyr Ala Glu Ala Arg Lys Arg Ile Leu Gly Ser Ala Ser Pro
      100            105            110
Glu Glu Glu Gln Glu Lys Pro Ile Leu Asp Arg Pro Thr Arg Ile Ser
      115            120            125
Gln Pro Glu Asp Ser Arg Gln Pro Asn Asn Val Ile Arg Gln Pro Leu
      130            135            140
Gly Pro Asp Gly Ser Gln Gly Phe Lys Gln Arg Arg
      145            150            155

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<210> 681

<211> 144

<212> PRT

<213> Homo sapiens

<400> 681

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Ser Ala Met Ala Ala Ala Ala Glu Gly Val Leu Ala Thr Arg Ser Asp
      1             5             10             15
Glu Pro Ala Arg Asp Asp Ala Ala Val Glu Thr Ala Glu Glu Ala Lys
      20             25             30
Glu Pro Ala Glu Ala Asp Ile Thr Glu Leu Cys Arg Asp Met Phe Ser
      35             40             45
Lys Met Ala Thr Tyr Leu Thr Gly Glu Leu Thr Ala Thr Ser Glu Asp
      50             55             60
Tyr Lys Leu Leu Glu Asn Met Asn Lys Leu Thr Ser Leu Lys Tyr Leu
      65             70             75             80

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621

Glu Met Lys Asp Ile Ala Ile Asn Ile Ser Arg Asn Leu Lys Asp Leu
 85 90 95
 Asn Gln Lys Tyr Ala Gly Leu Gln Pro Tyr Leu Asp Gln Ile Asn Val
 100 105 110
 Ile Glu Glu Gln Val Ala Ala Leu Glu Gln Ala Ala Tyr Lys Leu Asp
 115 120 125
 Ala Tyr Ser Lys Lys Leu Glu Ala Lys Tyr Lys Lys Leu Glu Lys Arg
 130 135 140

<210> 682

<211> 178

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (177)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 682

Arg Ala Trp Ser Pro Ser Gly Arg Ala Tyr Asp Pro Ala Asp Tyr Glu
 1 5 10 15
 His Leu Pro Val Ser Ala Glu Ile Lys Glu Leu Phe Gln Tyr Ile Ser
 20 25 30
 Arg Tyr Thr Pro Gln Leu Ile Asp Leu Asp His Lys Leu Lys Pro Phe
 35 40 45
 Ile Pro Asp Phe Ile Pro Ala Val Gly Asp Ile Asp Ala Phe Leu Lys
 50 55 60
 Val Pro Arg Pro Asp Gly Lys Pro Asp Asn Leu Gly Leu Leu Val Leu
 65 70 75 80
 Asp Glu Pro Ser Thr Lys Gln Ser Asp Pro Thr Val Leu Ser Leu Trp
 85 90 95
 Leu Thr Glu Asn Ser Lys Gln His Asn Ile Thr Gln His Met Lys Val
 100 105 110
 Lys Ser Leu Glu Asp Ala Glu Lys Asn Pro Lys Ala Ile Asp Thr Trp

Lys Asn Val Gln Ser Met Phe Gly Lys Leu Ile Asp Leu Ala Tyr Thr
 130 135 140
 Pro Phe His Ala Val Leu Lys Cys Gly His Leu Thr Ala Asp Val Gln
 145 150 155 160
 Val Phe Pro Arg Pro Glu Pro Phe Val Val Asp Glu Glu Ile Asp Pro
 165 170 175
 Ile Pro Lys Val Ile Asn Thr Asp Leu Glu Ile Val Gly Phe Ile Asp
 180 185 190
 Ile Ala Asp Ile Ser Ser Pro Pro Val Leu Ser Arg His Leu Val Leu
 195 200 205
 Pro Ile Ala Leu Asn Lys Glu Gly Asp Glu Val Gly Thr Gly Ile Thr
 210 215 220
 Asp Asp Asn Glu Asp Glu Asn Ser Ala Asn Gln Ile Ala Gly Lys Ile
 225 230 235 240
 Pro Asn Phe Cys Val Leu Leu His Gly Ser Leu Lys Val Glu Gly Met
 245 250 255
 Val Ala Ile Val Gln Leu Gly Pro Glu Trp His Gly Met Leu Tyr Ser
 260 265 270
 Gln Ala Asp Ser Lys Lys Lys Ser Asn Leu Met Met Ser Leu Phe Glu
 275 280 285
 Pro Gly Pro Glu Pro Leu Pro Trp Leu Gly Lys Met Ala Gln Leu Gly
 290 295 300
 Pro Ile Ser Asp Ala Lys Glu Asn Pro Tyr Gly Glu Asp Asp Asn Lys
 305 310 315 320
 Ser Pro Phe Pro Leu Gln Pro Lys Asn Lys Arg Ser Tyr Ala Gln Asn
 325 330 335
 Val Thr Val Trp Ile Lys Pro Ser Gly Leu Gln Thr Asp Val Gln Lys
 340 345 350
 Ile Leu Arg Asn Ala Arg Lys Leu Pro Glu Lys Thr Gln Thr Phe Tyr
 355 360 365
 Lys Glu Leu Asn Arg Leu Arg Lys Ala Ala Leu Ala Phe Gly Phe Leu
 370 375 380
 Asp Leu Leu Lys Gly Val Ala Asp Met Leu Glu Arg Glu Cys Thr Leu
 385 390 395 400

624

Leu Pro Glu Thr Ala His Pro Asp Ala Ala Phe Gln Leu Thr His Ala
 405 410 415

Ala Gln Gln Leu Lys Leu Ala Ser Thr Gly Thr Ser Glu Tyr Ala Ala
 420 425 430

Tyr Asp Gln Asn Ile Thr Pro Leu His Thr Asp Phe Ser Gly Ser Ser
 435 440 445

Thr Glu Arg Ile
 450

<210> 684

<211> 427

<212> PRT

<213> Homo sapiens

<400> 684

Thr Gly Ser Glu Phe Pro Gly Arg Pro Thr Arg Pro Gly Thr Lys Ala
 1 5 10 15

Gly Tyr Lys Leu Phe Ser Leu Ser Ser Val Glu Gln Leu Asp Gln Val
 20 25 30

His Gly Ser Asn Glu Ile Pro Asp Val Tyr Ile Val Glu Arg Leu Phe
 35 40 45

Ser Ser Ser Leu Val Val Val Val Ser His Thr Lys Pro Arg Gln Met
 50 55 60

Asn Val Tyr His Phe Lys Lys Gly Thr Glu Ile Cys Asn Tyr Ser Tyr
 65 70 75 80

Ser Ser Asn Ile Leu Ser Ile Arg Leu Asn Arg Gln Arg Leu Leu Val
 85 90 95

Cys Leu Glu Glu Ser Ile Tyr Ile His Asn Ile Lys Asp Met Lys Leu
 100 105 110

Leu Lys Thr Leu Leu Asp Ile Pro Ala Asn Pro Thr Gly Leu Cys Ala
 115 120 125

Leu Ser Ile Asn His Ser Asn Ser Tyr Leu Ala Tyr Pro Gly Ser Leu
 130 135 140

Thr Ser Gly Glu Ile Val Leu Tyr Asp Gly Asn Ser Leu Lys Thr Val
 145 150 155 160

Cys Thr Ile Ala Ala His Glu Gly Thr Leu Ala Ala Ile Thr Phe Asn

625

	165		170		175
Ala Ser Gly Ser Lys Leu Ala Ser Ala Ser Glu Lys Gly Thr Val Ile					
	180		185		190
Arg Val Phe Ser Val Pro Asp Gly Gln Lys Leu Tyr Glu Phe Arg Arg					
	195		200		205
Gly Met Lys Arg Tyr Val Thr Ile Ser Ser Leu Val Phe Ser Met Asp					
	210		215		220
Ser Gln Phe Leu Cys Ala Ser Ser Asn Thr Glu Thr Val His Ile Phe					
	225		230		235
Lys Leu Glu Gln Val Thr Asn Ser Arg Pro Glu Glu Pro Ser Thr Trp					
	245		250		255
Ser Gly Tyr Met Gly Lys Met Phe Met Ala Ala Thr Asn Tyr Leu Pro					
	260		265		270
Thr Gln Val Ser Asp Met Met His Gln Asp Arg Ala Phe Ala Thr Ala					
	275		280		285
Arg Leu Asn Phe Ser Gly Gln Arg Asn Ile Cys Thr Leu Ser Thr Ile					
	290		295		300
Gln Lys Leu Pro Arg Leu Leu Val Ala Ser Ser Ser Gly His Leu Tyr					
	305		310		315
Met Tyr Asn Leu Asp Pro Gln Asp Gly Gly Glu Cys Val Leu Ile Lys					
	325		330		335
Thr His Ser Leu Leu Gly Ser Gly Thr Thr Glu Glu Asn Lys Glu Asn					
	340		345		350
Asp Leu Arg Pro Ser Leu Pro Gln Ser Tyr Ala Ala Thr Val Ala Arg					
	355		360		365
Pro Ser Ala Ser Ser Ala Ser Thr Val Pro Gly Tyr Ser Glu Asp Gly					
	370		375		380
Gly Ala Leu Arg Gly Glu Val Ile Pro Glu His Glu Phe Ala Thr Gly					
	385		390		395
Pro Val Cys Leu Asp Asp Glu Asn Glu Phe Pro Pro Ile Ile Leu Cys					
	405		410		415
Arg Gly Asn Gln Lys Gly Lys Thr Lys Gln Ser					
	420		425		

626

<210> 685

<211> 321

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (154)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 685

Gly Gly Arg Ala Gly Gln Ser Lys Asp Ala Asp Leu Arg Pro Gly Asp
 1 5 10 15

Ile Ile Val Ala Ile Asn Gly Glu Ser Ala Glu Gly Met Leu His Ala
 20 25 30

Glu Ala Gln Ser Lys Ile Arg Gln Ser Pro Ser Pro Leu Arg Leu Gln
 35 40 45

Leu Asp Arg Ser Gln Ala Thr Ser Pro Gly Gln Thr Asn Gly Asp Ser
 50 55 60

Ser Leu Glu Val Leu Ala Thr Arg Phe Gln Gly Ser Val Arg Thr Tyr
 65 70 75 80

Thr Glu Ser Gln Ser Ser Leu Arg Ser Ser Tyr Ser Ser Pro Thr Ser
 85 90 95

Leu Ser Pro Arg Ala Gly Ser Pro Phe Ser Pro Pro Pro Ser Ser Ser
 100 105 110

Ser Leu Thr Gly Glu Ala Ala Ile Ser Arg Ser Phe Gln Ser Leu Ala
 115 120 125

Cys Ser Pro Gly Leu Pro Ala Ala Asp Arg Leu Ser Tyr Ser Gly Arg
 130 135 140

Pro Gly Ser Arg Gln Ala Gly Leu Gly Xaa Ala Gly Asp Ser Ala Val
 145 150 155 160

Leu Val Leu Pro Pro Ser Pro Gly Pro Arg Ser Ser Arg Pro Ser Met
 165 170 175

Asp Ser Glu Gly Gly Ser Leu Leu Leu Asp Glu Asp Ser Glu Val Phe
 180 185 190

Lys Met Leu Gln Glu Asn Arg Glu Gly Arg Ala Ala Pro Arg Gln Ser
 195 200 205

627

Ser Ser Phe Arg Leu Leu Gln Glu Ala Leu Glu Ala Glu Glu Arg Gly
 210 215 220
 Gly Thr Pro Ala Phe Leu Pro Ser Ser Leu Ser Pro Gln Ser Ser Leu
 225 230 235 240
 Pro Ala Ser Arg Ala Leu Ala Thr Pro Pro Lys Leu His Thr Cys Glu
 245 250 255
 Lys Cys Ser Thr Ser Ile Ala Asn Gln Ala Val Arg Ile Gln Glu Gly
 260 265 270
 Arg Tyr Arg His Pro Gly Cys Tyr Thr Cys Ala Asp Cys Gly Leu Asn
 275 280 285
 Leu Lys Met Arg Gly His Phe Trp Val Gly Asp Glu Leu Tyr Cys Glu
 290 295 300
 Lys His Ala Arg Gln Arg Tyr Ser Ala Pro Ala Thr Leu Ser Ser Arg
 305 310 315 320
 Ala

<210> 686

<211> 71

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (34)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 686

Phe His Pro Ser Tyr Trp Phe Val Cys Asn Glu Trp Leu Lys Ile Arg
 1 5 10 15

Val Ile Phe Tyr Pro Gln Met Arg Phe Cys Thr Phe Arg Ala Gly Leu
 20 25 30

Asn Xaa Phe Phe Phe Phe Leu Tyr Pro Asn Cys Trp Pro His Gly
 35 40 45

Asn Pro Phe Pro Asp Leu Cys Ser Thr Ile Tyr Trp Gln Asn Gly Arg
 50 55 60

Val Ala Ala Lys Gln Phe Val
 65 70

<210> 687

<211> 272

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (34)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 687

Ala Leu Gly Gly Phe Val Arg Leu Leu Pro Arg Cys Phe Gly Phe Pro
 1 5 10 15

Gly Ser Ser Ala Leu Phe Ser Pro Val Ala Ala Gly Ser Gly Arg Ser
 20 25 30

Ala Xaa Trp Asp Phe Leu Leu Ser Pro Glu Glu Phe Asn Thr Asn Met
 35 40 45

Asp Ile Arg Pro Asn His Thr Ile Tyr Ile Asn Asn Met Asn Asp Lys
 50 55 60

Ile Lys Lys Glu Glu Leu Lys Arg Ser Leu Tyr Ala Leu Phe Ser Gln
 65 70 75 80

Phe Gly His Val Val Asp Ile Val Ala Leu Lys Thr Met Lys Met Arg
 85 90 95

Gly Gln Ala Phe Val Ile Phe Lys Glu Leu Gly Ser Ser Thr Asn Ala
 100 105 110

Leu Arg Gln Leu Gln Gly Phe Pro Phe Tyr Gly Lys Pro Met Arg Ile
 115 120 125

Gln Tyr Ala Lys Thr Asp Ser Asp Ile Ile Ser Lys Met Arg Gly Thr
 130 135 140

Phe Ala Asp Lys Glu Lys Lys Lys Glu Lys Lys Lys Ala Lys Thr Val
 145 150 155 160

Glu Gln Thr Ala Thr Thr Thr Asn Lys Lys Pro Gly Gln Gly Thr Pro
 165 170 175

Asn Ser Ala Asn Thr Gln Gly Asn Ser Thr Pro Asn Pro Gln Val Pro
 180 185 190

Asp Tyr Pro Pro Asn Tyr Ile Leu Phe Leu Asn Asn Leu Pro Glu Glu

195	200	205
Thr Asn Glu Met Met Leu Ser Met Leu Phe Asn Gln Phe Pro Gly Phe		
210	215	220
Lys Glu Val Arg Leu Val Pro Gly Arg His Asp Ile Ala Phe Val Glu		
225	230	235 240
Phe Glu Asn Asp Gly Gln Ala Gly Ala Ala Arg Asp Ala Leu Gln Gly		
245	250	255
Phe Lys Ile Thr Pro Ser His Ala Met Lys Ile Thr Tyr Ala Lys Lys		
260	265	270

<210> 688

<211> 173

<212> PRT

<213> Homo sapiens

<400> 688

His Leu Phe Cys Arg Ile Val Lys Asn Glu Val Leu Phe Leu Glu Tyr
1 5 10 15
Leu Thr Gly Cys Leu Ala Ser Arg Arg Cys Leu Ala Lys Ala Leu Pro
20 25 30
Glu Met Asp Ser Arg Ile Pro Tyr Asp Asp Tyr Pro Val Val Phe Leu
35 40 45
Pro Ala Tyr Glu Asn Pro Pro Ala Trp Ile Pro Pro His Glu Arg Val
50 55 60
His His Pro Asp Tyr Asn Asn Glu Leu Thr Gln Phe Leu Pro Arg Thr
65 70 75 80
Ile Thr Leu Lys Lys Pro Pro Gly Ala Gln Leu Gly Phe Asn Ile Arg
85 90 95
Gly Gly Lys Ala Ser Gln Leu Gly Ile Phe Ile Ser Lys Val Ile Pro
100 105 110
Asp Ser Asp Ala His Arg Ala Gly Leu Gln Glu Gly Asp Gln Val Leu
115 120 125
Ala Val Asn Asp Val Asp Phe Gln Asp Ile Glu His Ser Lys Ala Val
130 135 140

630

Glu Ile Leu Lys Thr Ala Arg Glu Ile Ser Met Arg Val Arg Phe Phe
145 150 155 160

Pro Tyr Asn Tyr His Arg Gln Lys Glu Arg Thr Val His
 165 170

<210> 689

<211> 66

<212> PRT

<213> Homo sapiens

<400> 689

Val Thr Glu Arg Gly Ala Arg Gly Arg Ala Arg Ser Ile Pro Leu Ser
1 5 10 15

Leu Glu Glu Thr Thr Ala Ser Asp Leu Arg Cys Gly Arg Gly Arg Gln
 20 25 30

Val Pro Ser Val Glu Gly Gln His Ala Gly Ser Thr Trp Gly Gly Gly
 35 40 45

Ala Leu Arg Asp Ser Arg Cys Asn Trp Asp Arg Ser Arg Glu Leu Gln
 50 55 60

Phe Pro
65

<210> 690

<211> 94

<212> PRT

<213> Homo sapiens

<400> 690

Gly Arg Gly Phe Leu Ser His Lys Asn Glu Ile Leu Glu Ile Ala Leu
1 5 10 15

Asp Gln Lys Gly Leu Thr Asn Asp Arg Lys Ile Ala Phe Ile Asp Lys
 20 25 30

Asn Arg Asp Leu Cys Ile Thr Ser Val Lys Gly Phe Gly Lys Glu Glu
 35 40 45

Gln Ile Ile Lys Leu Gly Asn Asn Gly Ala Tyr Phe Gly Met Glu Arg
 50 55 60

Tyr Met Gln Tyr Pro Leu Trp Thr Ser Arg Tyr Ser Ile Tyr Ser Val

631

65	70	75	80
Val	Leu	Pro	Gln
Tyr	Ser	Leu	Cys
Gly	Gln	Arg	His
Phe	Ala		
	85	90	

<210> 691

<211> 66

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (38)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (46)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (50)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (51)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (53)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 691

Asn	Gln	Asn	Gly	Val	His	Val	Ile	Leu	Phe	Asp	Ile	Ser	Ser	Pro	Ala
1		5					10					15			

Gln	Thr	Ile	Pro	Glu	Gly	Ile	Lys	Phe	Ile	Gln	Gly	Asp	Ile	Arg	His
	20					25							30		

Leu	Ser	Asp	Val	Glu	Xaa	Ser	Leu	Pro	Gly	Cys	Arg	Arg	Xaa	Leu	Cys
	35						40						45		

Val	Xaa	Xaa	Leu	Xaa	Leu	Met	Val	Met	Phe	Arg	Ala	Gly	Ala	Asn	Ser
	50					55							60		

Ile Glu

632

65

<210> 692

<211> 124

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (88)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 692

Thr Lys Gln Gly Glu Lys Lys Glu Leu Gly Gln Asn Arg Arg Arg Phe
 1 5 10 15

Pro Thr Arg Ile His Pro Arg Pro Arg Asp Thr Gln Ser Pro His Pro
 20 25 30

Gln Pro Ala Arg Ala Ser Arg Pro Gln Leu Leu Ala Leu Gly Thr Ala
 35 40 45

Gly Ser Pro Ala Arg Thr Arg His Lys Ala Asp Gln Ser Arg Arg Arg
 50 55 60

Gly Gly Gly Gly Thr Thr Arg Arg Gly Phe Pro Gly Arg Cys Ser Pro
 65 70 75 80

Pro Ala Ala Pro Ser Leu Gly Xaa Gly Gly Arg Leu Val Trp Phe Ser
 85 90 95

Arg Pro Leu Ala Pro Thr Pro Thr Pro Pro Lys Gln Asn Arg Pro Pro
 100 105 110

Ser Leu Gly Trp Arg Thr Arg Leu Leu Ala Ala Ser
 115 120

<210> 693

<211> 56

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (22)

<223> Xaa equals any of the naturally occurring L-amino acids

633

<220>

<221> SITE

<222> (32)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (39)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 693

Ser Met Arg Thr Glu Ile Ser Val Leu Tyr Arg Leu Pro Ser Leu Cys
1 5 10 15

Cys Ser Val Ile Leu Xaa Lys Gln Met Glu Thr Asp Gly Ser Ala Xaa
20 25 30

Ser Thr Arg Gly Thr Glu Xaa Arg Gly Glu Val Ser Pro Ala Ile Ala
35 40 45

Asn Gln Ala Arg Gly Gly Gly Gly
50 55

<210> 694

<211> 70

<212> PRT

<213> Homo sapiens

<400> 694

Val Thr Ser Ser Cys Thr Leu Arg Glu Gly Ser Ser Ser Cys Ser Gln
1 5 10 15

Ser Val Ala Leu Lys Thr Ser Glu Ser Arg Ala Leu Pro Pro Glu Arg
20 25 30

Glu Gly Glu Gln Lys Glu Lys Pro Arg Ala Gly Arg Ala Cys Phe Val
35 40 45

Cys Trp Phe Gly Phe Phe Ser Phe Ile Phe Phe Phe Arg Glu Asp Ser
50 55 60

Phe Lys Leu Ser Ser Lys
65 70

<210> 695

<211> 273

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (27)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (28)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (34)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 695

Gly Arg Val Gly Met Leu Arg Leu Leu Ser Ser Leu Leu Leu Val Ala
1 5 10 15

Val Ala Ser Gly Tyr Gly Pro Pro Ser Ser Xaa Xaa Ser Ser Arg Val
20 25 30

Val Xaa Gly Glu Asp Ala Val Pro Tyr Ser Trp Pro Trp Gln Val Ser
35 40 45

Leu Gln Tyr Glu Lys Ser Gly Ser Phe Tyr His Thr Cys Gly Gly Ser
50 55 60

Leu Ile Ala Pro Asp Trp Val Val Thr Ala Gly His Cys Ile Ser Arg
65 70 75 80

Asp Leu Thr Tyr Gln Val Val Leu Gly Glu Tyr Asn Leu Ala Val Lys
85 90 95

Glu Gly Pro Glu Gln Val Ile Pro Ile Asn Ser Glu Glu Leu Phe Val
100 105 110

His Pro Leu Trp Asn Arg Ser Cys Val Ala Cys Gly Asn Asp Ile Ala
115 120 125

Leu Ile Lys Leu Ser Arg Ser Ala Gln Leu Gly Asp Ala Val Gln Leu
130 135 140

Ala Ser Leu Pro Pro Ala Gly Asp Ile Leu Pro Asn Lys Thr Pro Cys
145 150 155 160

Tyr Ile Thr Gly Trp Gly Arg Leu Tyr Thr Asn Gly Pro Leu Pro Asp
165 170 175

635

Lys Leu Gln Gln Ala Arg Leu Pro Val Val Asp Tyr Lys His Cys Ser
 180 185 190

Arg Trp Asn Trp Trp Gly Ser Thr Val Lys Lys Thr Met Val Cys Ala
 195 200 205

Gly Gly Tyr Ile Arg Ser Gly Cys Asn Gly Asp Ser Gly Gly Pro Leu
 210 215 220

Asn Cys Pro Thr Glu Asp Gly Gly Trp Gln Val His Gly Val Thr Ser
 225 230 235 240

Phe Val Ser Gly Phe Gly Cys Asn Phe Ile Trp Lys Pro Thr Val Phe
 245 250 255

Thr Arg Val Ser Ala Phe Ile Asp Trp Ile Glu Glu Thr Ile Ala Ser
 260 265 270

His

<210> 696

<211> 180

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (43)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (157)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (158)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (162)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (163)

636

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 696

Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu Ser His Asn Cys Gly
 1 5 10 15

His His Glu Asp Ala Gly Val Ile Cys Ser Ala Ser Gln Ser Gln Pro
 20 25 30

Thr Pro Ser Pro Asp Thr Trp Pro Thr Ser Xaa Ala Ser Thr Ala Gly
 35 40 45

Ser Glu Ser Thr Leu Ala Leu Arg Leu Val Asn Gly Gly Asp Arg Cys
 50 55 60

Arg Gly Arg Val Glu Val Leu Tyr Gln Gly Ser Trp Gly Thr Val Cys
 65 70 75 80

Asp Asp Tyr Trp Asp Thr Asn Asp Ala Asn Val Val Cys Arg Gln Leu
 85 90 95

Gly Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Gln Phe Gly Gln
 100 105 110

Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys Ser Gly His Glu
 115 120 125

Ser Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu Ser His Asn Cys
 130 135 140

Gly His His Glu Asp Ala Gly Val Ile Cys Ser Ala Xaa Xaa Val Pro
 145 150 155 160

Val Xaa Xaa Gln Ala Arg Tyr Leu Ala Asp His Gln Leu Thr Gly Ile
 165 170 175

Asp Ser Arg Ile
 180

<210> 697

<211> 62

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (44)

<223> Xaa equals any of the naturally occurring L-amino acids

637

<220>

<221> SITE

<222> (57)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 697

Val	Pro	Cys	Pro	Pro	Gly	His	Phe	Pro	Pro	Met	Ser	Pro	Asp	Phe	Thr
1				5					10					15	

Val	Phe	Met	Ile	Lys	Tyr	Leu	Met	Thr	Met	Ile	Val	Gly	Ile	Thr	Thr
			20					25					30		

Gly	Phe	Trp	Ile	Trp	Ser	Gly	Lys	Thr	Leu	Gln	Xaa	Trp	Arg	Arg	Phe
		35					40					45			

Tyr	His	Arg	Leu	Ser	His	Ser	Ser	Xaa	Gly	Glu	Thr	Ala	Val
	50					55					60		

<210> 698

<211> 134

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (121)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (124)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 698

Phe	Phe	Arg	Ser	Ser	Ser	Asp	Asn	Gly	Ser	Pro	Ile	Arg	Gln	Tyr	Glu
1				5					10					15	

Leu	Gln	Pro	Gln	His	Thr	Arg	Gly	Gln	Leu	Trp	Ala	Trp	Lys	Gln	Glu
			20					25					30		

Pro	Arg	Asn	Ser	Gln	Leu	Arg	Ile	Val	Leu	Val	Gly	Lys	Thr	Gly	Ala
		35					40					45			

Gly	Lys	Ser	Ala	Thr	Gly	Asn	Ser	Ile	Leu	Gly	Arg	Lys	Val	Phe	His
	50					55					60				

Ser	Gly	Thr	Ala	Ala	Lys	Ser	Ile	Thr	Lys	Lys	Cys	Glu	Lys	Arg	Ser
	65				70					75					80

638

Ser Ser Trp Lys Glu Thr Glu Leu Val Val Val Asp Thr Pro Gly Ile
 85 90 95

Phe Asp Thr Glu Val Pro Asn Ala Glu Thr Ser Lys Glu Ile Ile Arg
 100 105 110

Cys Ile Leu Leu Thr Ser Pro Gly Xaa His Ala Xaa Ala Ser Gly Gly
 115 120 125

Ser Thr Gly Pro Leu His
 130

<210> 699

<211> 371

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (32)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 699

Asp Gln Phe Ser Arg Ser Leu Asn Asn Ser Ala Thr Val Gln His Val
 1 5 10 15

Gln Lys Leu Trp Gln Pro Arg Gly Cys Thr Arg Thr Arg Arg Trp Xaa
 20 25 30

Ala Glu Glu Arg Gly Arg Glu Pro Gln Gly Gln Ala Gly Gly Gly Ala
 35 40 45

Ser Gln Ala Ala Arg Cys Gly Ala Ala Pro Gly Gly Gly Arg Val Glu
 50 55 60

Ala Leu Gly Gln Phe Val Met Lys Thr Arg Arg Thr Leu Lys Gly His
 65 70 75 80

Gly Asn Lys Val Leu Cys Met Asp Trp Cys Lys Asp Lys Arg Arg Ile
 85 90 95

Val Ser Ser Ser Gln Asp Gly Lys Val Ile Val Trp Asp Ser Phe Thr
 100 105 110

Thr Asn Lys Glu His Ala Val Thr Met Pro Cys Thr Trp Val Met Ala
 115 120 125

Cys Ala Tyr Ala Pro Ser Gly Cys Ala Ile Ala Cys Gly Gly Leu Asp
 130 135 140

639

Asn Lys Cys Ser Val Tyr Pro Leu Thr Phe Asp Lys Asn Glu Asn Met
 145 150 155 160

Ala Ala Lys Lys Lys Ser Val Ala Met His Thr Asn Tyr Leu Ser Ala
 165 170 175

Cys Ser Phe Thr Asn Ser Asp Met Gln Ile Leu Thr Ala Ser Gly Asp
 180 185 190

Gly Thr Cys Ala Leu Trp Asp Val Glu Ser Gly Gln Leu Leu Gln Ser
 195 200 205

Phe His Gly His Gly Ala Asp Val Leu Cys Leu Asp Leu Ala Pro Ser
 210 215 220

Glu Thr Gly Asn Thr Phe Val Ser Gly Gly Cys Asp Lys Lys Ala Met
 225 230 235 240

Val Trp Asp Met Arg Ser Gly Gln Cys Val Gln Ala Phe Glu Thr His
 245 250 255

Glu Ser Asp Ile Asn Ser Val Arg Tyr Tyr Pro Ser Gly Asp Ala Phe
 260 265 270

Ala Ser Gly Ser Asp Asp Ala Thr Cys Arg Leu Tyr Asp Leu Arg Ala
 275 280 285

Asp Arg Glu Val Ala Ile Tyr Ser Lys Glu Ser Ile Ile Phe Gly Ala
 290 295 300

Ser Ser Val Asp Phe Ser Leu Ser Gly Arg Leu Leu Phe Ala Gly Tyr
 305 310 315 320

Asn Asp Tyr Thr Ile Asn Val Trp Asp Val Leu Lys Gly Ser Arg Val
 325 330 335

Ser Ile Leu Phe Gly His Glu Asn Arg Val Ser Thr Leu Arg Val Ser
 340 345 350

Pro Asp Gly Thr Ala Phe Cys Ser Gly Ser Trp Asp His Thr Leu Arg
 355 360 365

Val Trp Ala
 370

<210> 700

<211> 200

<212> PRT

640

<213> Homo sapiens

<400> 700

Ser Gln Ala Pro Pro Pro Pro Pro Pro Ser Arg Pro Gly Pro Pro
1 5 10 15

Pro Leu Pro Pro Ser Ser Ser Gly Asn Asp Glu Thr Pro Arg Leu Pro
20 25 30

Gln Arg Asn Leu Ser Leu Ser Ser Ser Thr Pro Pro Leu Pro Ser Pro
35 40 45

Gly Arg Ser Gly Pro Leu Pro Pro Pro Pro Ser Glu Arg Pro Pro Pro
50 55 60

Pro Val Arg Asp Pro Pro Gly Arg Ser Gly Pro Leu Pro Pro Pro Pro
65 70 75 80

Pro Val Ser Arg Asn Gly Ser Thr Ser Arg Ala Leu Pro Ala Thr Pro
85 90 95

Gln Leu Pro Ser Arg Ser Gly Val Asp Ser Pro Arg Ser Gly Pro Arg
100 105 110

Pro Pro Leu Pro Pro Asp Arg Pro Ser Ala Gly Ala Pro Pro Pro Pro
115 120 125

Pro Pro Ser Thr Ser Ile Arg Asn Gly Phe Gln Asp Ser Pro Cys Glu
130 135 140

Asp Glu Trp Glu Ser Arg Phe Tyr Phe His Pro Ile Ser Asp Leu Pro
145 150 155 160

Pro Pro Glu Pro Tyr Val Gln Thr Thr Lys Ser Tyr Pro Ser Lys Leu
165 170 175

Ala Arg Asn Glu Ser Arg Ser Gly Ser Asn Arg Arg Glu Arg Gly Ala
180 185 190

Pro Pro Leu Pro Pro Ile Pro Arg
195 200

<210> 701

<211> 660

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (47)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (397)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 701

His Tyr Phe Tyr Leu Lys Glu Arg Ile Leu Glu Leu Thr Leu Gln Arg
 1 5 10 15

Arg Lys Met Val Val Ser Glu Val Asp Ile Ala Lys Ala Asp Pro Ala
 20 25 30

Ala Ala Ser His Pro Leu Leu Leu Asn Gly Asp Ala Thr Val Xaa Gln
 35 40 45

Lys Asn Pro Gly Ser Val Ala Glu Asn Asn Leu Cys Ser Gln Tyr Glu
 50 55 60

Glu Lys Val Arg Pro Cys Ile Asp Leu Ile Asp Ser Leu Arg Ala Leu
 65 70 75 80

Gly Val Glu Gln Asp Leu Ala Leu Pro Ala Ile Ala Val Ile Gly Asp
 85 90 95

Gln Ser Ser Gly Lys Ser Ser Val Leu Glu Ala Leu Ser Gly Val Ala
 100 105 110

Leu Pro Arg Gly Ser Gly Ile Val Thr Arg Cys Pro Leu Val Leu Lys
 115 120 125

Leu Lys Lys Leu Val Asn Glu Asp Lys Trp Arg Gly Lys Val Ser Tyr
 130 135 140

Gln Asp Tyr Glu Ile Glu Ile Ser Asp Ala Ser Glu Val Glu Lys Glu
 145 150 155 160

Ile Asn Lys Ala Gln Asn Ala Ile Ala Gly Glu Gly Met Gly Ile Ser
 165 170 175

His Glu Leu Ile Thr Leu Glu Ile Ser Ser Arg Asp Val Pro Asp Leu
 180 185 190

Thr Leu Ile Asp Leu Pro Gly Ile Thr Arg Val Ala Val Gly Asn Gln
 195 200 205

Pro Ala Asp Il Gly Tyr Lys Ile Lys Thr Leu Ile Lys Lys Tyr Ile
 210 215 220

Gln Arg Gln Glu Thr Ile Ser Leu Val Val Val Pro Ser Asn Val Asp
 225 230 235 240
 Ile Ala Thr Thr Glu Ala Leu Ser Met Ala Gln Glu Val Asp Pro Glu
 245 250 255
 Gly Asp Arg Thr Ile Gly Ile Leu Thr Lys Pro Asp Leu Val Asp Lys
 260 265 270
 Gly Thr Glu Asp Lys Val Val Asp Val Val Arg Asn Leu Val Phe His
 275 280 285
 Leu Lys Lys Gly Tyr Met Ile Val Lys Cys Arg Gly Gln Gln Glu Ile
 290 295 300
 Gln Asp Gln Leu Ser Leu Ser Glu Ala Leu Gln Arg Glu Lys Ile Phe
 305 310 315 320
 Phe Glu Asn His Pro Tyr Phe Arg Asp Leu Leu Glu Glu Gly Lys Ala
 325 330 335
 Thr Val Pro Cys Leu Ala Glu Lys Leu Thr Ser Glu Leu Ile Thr His
 340 345 350
 Ile Cys Lys Ser Leu Pro Leu Leu Glu Asn Gln Ile Lys Glu Thr His
 355 360 365
 Gln Arg Ile Thr Glu Glu Leu Gln Lys Tyr Gly Val Asp Ile Pro Glu
 370 375 380
 Asp Glu Asn Glu Lys Met Phe Phe Leu Ile Asp Lys Xaa Asn Ala Phe
 385 390 395 400
 Asn Gln Asp Ile Thr Ala Leu Met Gln Gly Glu Glu Thr Val Gly Glu
 405 410 415
 Glu Asp Ile Arg Leu Phe Thr Arg Leu Arg His Glu Phe His Lys Trp
 420 425 430
 Ser Thr Ile Ile Glu Asn Asn Phe Gln Glu Gly His Lys Ile Leu Ser
 435 440 445
 Arg Lys Ile Gln Lys Phe Glu Asn Gln Tyr Arg Gly Arg Glu Leu Pro
 450 455 460
 Gly Phe Val Asn Tyr Arg Thr Phe Glu Thr Ile Val Lys Gln Gln Ile
 465 470 475 480
 Lys Ala Leu Glu Glu Pro Ala Val Asp Met Leu His Thr Val Thr Asp
 485 490 495

643

Met Val Arg Leu Ala Phe Thr Asp Val Ser Ile Lys Asn Phe Glu Glu
500 505 510

Phe Phe Asn Leu His Arg Thr Ala Lys Ser Lys Ile Glu Asp Ile Arg
515 520 525

Ala Glu Gln Glu Arg Glu Gly Glu Lys Leu Ile Arg Leu His Phe Gln
530 535 540

Met Glu Gln Ile Val Tyr Cys Gln Asp Gln Val Tyr Arg Gly Ala Leu
545 550 555 560

Gln Lys Val Arg Glu Lys Glu Leu Glu Glu Lys Lys Lys Lys Ser
565 570 575

Trp Asp Phe Gly Ala Phe Gln Ser Ser Ser Ala Thr Asp Ser Ser Met
580 585 590

Glu Glu Ile Phe Gln His Leu Met Ala Tyr His Gln Glu Ala Ser Lys
595 600 605

Arg Ile Ser Ser His Ile Pro Leu Ile Ile Gln Phe Phe Met Leu Gln
610 615 620

Thr Tyr Gly Gln Gln Leu Gln Lys Ala Met Leu Gln Leu Leu Gln Asp
625 630 635 640

Lys Asp Thr Tyr Ser Trp Leu Leu Lys Glu Arg Ser Asp Pro Ala Thr
645 650 655

Ser Gly Ser Ser
660

<210> 702

<211> 74

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (13)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (36)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 702

644

Glu His Tyr Ser Tyr Pro Cys Thr Pro Thr Thr Met Xaa Pro Arg Ser
 1 5 10 15
 Ala Tyr Trp His His Ile Thr Gly Ser Gln Asn Ile Ala Glu Ala Ser
 20 25 30
 Ser Tyr Ala Xaa Glu Gly Tyr Gly Ala Ala Gln Ala Ser Ser Glu Thr
 35 40 45
 Asp Leu Leu Asn Arg Phe Ile Leu Leu Lys Pro Lys Pro Ser Gln Gly
 50 55 60
 Asp Ser Ser Glu Ala Lys Thr Pro Ser Gln
 65 70

<210> 703
 <211> 284
 <212> PRT
 <213> Homo sapiens

<400> 703
 Glu Ala Ala Pro Trp Leu Glu Ala Ala Ser Val Cys Ala Val Thr Ile
 1 5 10 15
 Ile Asn Pro His Ser Ala Pro Ser Pro Asp Ala Leu Val Thr Gly Ala
 20 25 30
 Ser Trp Met Ser Asn His Val Val Gly Gly Cys Arg Leu Arg Ala Ser
 35 40 45
 Val Gly Ser Ser Thr Thr Val Ser Val Gly Ser Gly His Gly Thr Leu
 50 55 60
 Ser Pro Ser Cys Thr Trp Ser Arg Val His Ser His Pro Pro Ser Cys
 65 70 75 80
 Gly Glu Arg Leu Ala Arg Pro Gly Gln Ala Arg Gln Lys Val Ser Ala
 85 90 95
 Lys Trp Pro Arg Pro His Pro Ala Ile Ser Gln Leu Leu Phe Ile Thr
 100 105 110
 Phe Val Pro His Leu Gly Val Cys Phe Leu His Leu Asp Thr Leu Pro
 115 120 125
 Gly Arg Ser Ser Glu Pro Asn Pro Arg Leu Cys Ser Val Gly Glu Gly
 130 135 140
 Met Thr Ser Pro Pro Pro Asp Leu Pro Arg Val Leu Val Ser Leu Ser

645

145		150		155		160
Ala Gly Gly Pro	Leu Cys Val Phe Val	Gln Phe Cys Cys Met Gly Phe				
	165	170	175			
Val Thr Gln Lys	Leu Met Leu Arg Lys	Ala Ser Leu Gly Pro Leu Pro				
	180	185	190			
Arg Ala Ser Glu	Arg Pro Gly Val Pro Val Phe	Leu Glu Met Gly Pro				
	195	200	205			
Ser Ala Ala Gly	Cys Glu Ala Leu Arg Ser Ile Thr	Gly Arg Ala Trp				
	210	215	220			
Arg Trp Trp Pro	Pro Gly Thr Thr Leu Ser Cys Leu Phe Thr Phe His					
	225	230	235	240		
Tyr Gln Val Phe	Ser Gly His Tyr Asp Leu Phe Pro Tyr Asn Ser Asp					
	245	250	255			
Leu Cys Ile Leu	Leu Trp Pro Ala Val Ser Ala Gly Gly Ser Gln Arg					
	260	265	270			
Gly Thr Gly Arg	Ala Ser Pro Cys Arg Thr Ala Glu					
	275	280				

<210> 704
 <211> 339
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (7)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (21)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (24)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (57)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 704

Gly	Arg	Ile	Gly	Val	His	Xaa	Pro	Phe	Lys	Trp	Ser	Ser	Phe	Thr	Pro
1				5					10					15	
Pro	Arg	Pro	Ser	Xaa	Ser	Trp	Xaa	Leu	Val	Arg	Arg	Ser	Leu	Met	Ala
			20				25						30		
Pro	Val	Gln	Gly	Gly	Val	Arg	Val	Ile	Val	Gln	Pro	Pro	Glu	Asp	Cys
		35					40					45			
Gly	Ser	Gly	Leu	Gln	Leu	Phe	Gln	Xaa	Phe	Thr	Val	His	Arg	Ser	Pro
	50					55					60				
Val	Thr	Lys	Ile	Met	Leu	Ser	Glu	Lys	His	Leu	Ile	Ser	Val	Cys	Ala
65					70					75					80
Asp	Asn	Asn	His	Val	Arg	Thr	Trp	Ser	Val	Thr	Arg	Phe	Arg	Gly	Met
			85						90					95	
Ile	Ser	Thr	Gln	Pro	Gly	Ser	Thr	Pro	Leu	Ala	Ser	Phe	Lys	Ile	Leu
			100					105					110		
Ala	Leu	Glu	Ser	Ala	Asp	Gly	His	Gly	Gly	Cys	Ser	Ala	Gly	Asn	Asp
		115					120					125			
Ile	Gly	Pro	Tyr	Gly	Glu	Arg	Asp	Asp	Gln	Gln	Val	Phe	Ile	Gln	Lys
	130					135					140				
Val	Val	Pro	Ser	Ala	Ser	Gln	Leu	Phe	Val	Arg	Leu	Ser	Ser	Thr	Gly
145					150					155					160
Gln	Arg	Val	Cys	Ser	Val	Arg	Ser	Val	Asp	Gly	Ser	Pro	Thr	Thr	Ala
			165						170					175	
Phe	Thr	Val	Leu	Glu	Cys	Glu	Gly	Ser	Arg	Arg	Leu	Gly	Ser	Arg	Pro
		180					185						190		
Arg	Arg	Tyr	Leu	Leu	Thr	Gly	Gln	Ala	Asn	Gly	Ser	Leu	Ala	Met	Trp
		195					200					205			
Asp	Leu	Thr	Thr	Ala	Met	Asp	Gly	Leu	Gly	Gln	Ala	Pro	Ala	Gly	Gly
	210					215					220				
Leu	Thr	Glu	Gln	Glu	Leu	Met	Glu	Gln	Leu	Glu	His	Cys	Glu	Leu	Ala
225					230					235					240
Pro	Pro	Ala	Pro	Ser	Ala	Pro	Ser	Trp	Gly	Cys	Leu	Pro	Ser	Pro	Ser
					245				250					255	

647

Pro Arg Ile Ser Leu Thr Ser Leu His Ser Ala Ser Ser Asn Thr Ser
 260 265 270

Leu Ser Gly His Arg Gly Ser Pro Ser Pro Pro Gln Ala Glu Ala Arg
 275 280 285

Arg Arg Gly Gly Gly Ser Phe Val Glu Arg Cys Gln Glu Leu Val Arg
 290 295 300

Ser Gly Pro Asp Leu Arg Arg Pro Pro Thr Pro Ala Pro Trp Pro Ser
 305 310 315 320

Ser Gly Leu Gly Thr Pro Leu Thr Pro Pro Lys Met Lys Leu Asn Glu
 325 330 335

Thr Ser Phe

<210> 705

<211> 104

<212> PRT

<213> Homo sapiens

<400> 705

Pro Lys Phe Arg Thr Ile Gly Ile Val Cys Leu Lys Asn Thr Tyr Lys
 1 5 10 15

Lys Thr Leu Val Asn Ile Leu Val Met Leu Glu Arg Lys Val Leu Leu
 20 25 30

Pro Leu Arg Leu Cys Ala Gly Ala Tyr Gly Ser Lys Val Val Tyr Cys
 35 40 45

Pro Phe Ser Ala Ser Pro Gly Asn Asp Arg His Tyr Ser Pro Ile Gly
 50 55 60

Leu Pro Ser Leu Tyr Arg Lys Thr Lys Gln Ala Pro Leu Ala Lys Arg
 65 70 75 80

Tyr Gly Ile Trp Gln Ser Glu Phe Ser Val Ile Trp Lys Val Lys Glu
 85 90 95

Leu Val Pro Val Ser Pro Phe Ser
 100

<210> 706

<211> 339

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (2)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (37)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (173)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (293)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 706

Lys	Xaa	Ser	Phe	Leu	Lys	Ala	Leu	Leu	Ala	Thr	Phe	Gly	Ser	Ser	Phe
1				5					10					15	

Leu	Ile	Ser	Ala	Cys	Phe	Lys	Leu	Ile	Gln	Asp	Leu	Leu	Ser	Phe	Ile
			20					25					30		

Asn	Pro	Gln	Leu	Xaa	Ser	Ile	Leu	Ile	Arg	Phe	Ile	Ser	Asn	Pro	Met
		35					40					45			

Ala	Pro	Ser	Trp	Trp	Gly	Phe	Leu	Val	Ala	Gly	Leu	Met	Phe	Leu	Cys
		50			55						60				

Ser	Met	Met	Gln	Ser	Leu	Ile	Leu	Gln	His	Tyr	Tyr	His	Tyr	Ile	Phe
65					70				75					80	

Val	Thr	Gly	Val	Lys	Phe	Arg	Thr	Gly	Ile	Met	Gly	Val	Ile	Tyr	Arg
			85						90					95	

Lys	Ala	Leu	Val	Ile	Thr	Asn	Ser	Val	Lys	Arg	Ala	Ser	Thr	Val	Gly
		100						105					110		

Glu	Ile	Val	Asn	Leu	Met	Ser	Val	Asp	Ala	Gln	Arg	Phe	Met	Asp	Leu
		115					120					125			

Ala	Pro	Phe	Leu	Asn	Leu	Leu	Trp	Ser	Ala	Pro	Leu	Gln	Ile	Ile	Leu
		130				135						140			

Ala Ile Tyr Phe Leu Trp Gln Asn Leu Gly Pro Ser Val Leu Ala Gly
 145 150 155 160
 Val Ala Phe Met Val Leu Leu Ile Pro Leu Asn Gly Xaa Val Ala Val
 165 170 175
 Lys Met Arg Ala Phe Gln Val Lys Gln Met Lys Leu Lys Asp Ser Arg
 180 185 190
 Ile Lys Leu Met Ser Glu Ile Leu Asn Gly Ile Lys Val Leu Lys Leu
 195 200 205
 Tyr Ala Trp Glu Pro Ser Phe Leu Lys Gln Val Glu Gly Ile Arg Gln
 210 215 220
 Gly Glu Leu Gln Leu Leu Arg Thr Ala Ala Tyr Leu His Thr Thr Thr
 225 230 235 240
 Thr Phe Thr Trp Met Cys Ser Pro Phe Leu Val Thr Leu Ile Thr Leu
 245 250 255
 Trp Val Tyr Val Tyr Val Asp Pro Asn Asn Val Leu Asp Ala Glu Lys
 260 265 270
 Ala Phe Val Ser Val Ser Leu Val Asn Ile Leu Arg Leu Pro Leu Asn
 275 280 285
 Met Leu Pro Gln Xaa Ile Ser Asn Leu Thr Gln Ala Ser Val Ser Leu
 290 295 300
 Lys Arg Ile Gln Gln Phe Leu Ser Gln Glu Glu Leu Asp Pro Gln Ser
 305 310 315 320
 Val Glu Arg Lys Thr Ser Ser Gln Ala Met His Thr Ile His Ser Gly
 325 330 335
 Thr Phe Thr

<210> 707

<211> 117

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (1)

<223> Xaa equals any of the naturally occurring L-amino acids

650

<220>

<221> SITE

<222> (8)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (31)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 707

Xaa	Ala	Leu	Gly	Val	Glu	Glu	Xaa	Ala	Asp	Phe	Gln	Ser	Leu	Cys	Ser
1				5					10					15	

Trp	Tyr	His	Gly	Ala	Ile	Ser	Arg	Thr	Asp	Ala	Glu	Asn	Leu	Xaa	Arg
			20					25					30		

Leu	Cys	Lys	Glu	Ala	Ser	Tyr	Leu	Val	Arg	Asn	Ser	Glu	Thr	Ser	Lys
		35					40					45			

Asn	Asp	Phe	Ser	Leu	Ser	Leu	Lys	Ser	Ser	Gln	Gly	Phe	Met	His	Met
	50					55					60				

Lys	Leu	Ser	Arg	Thr	Lys	Glu	His	Lys	Tyr	Val	Leu	Gly	Gln	Asn	Ser
65					70					75				80	

Pro	Pro	Phe	Ser	Ser	Val	Pro	Glu	Ile	Val	His	His	Tyr	Ala	Ser	Arg
				85					90					95	

Lys	Leu	Pro	Ile	Lys	Gly	Ala	Glu	His	Met	Ser	Leu	Leu	Tyr	Pro	Val
		100						105					110		

Ala	Ile	Arg	Thr	Leu
				115

<210> 708

<211> 199

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (66)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 708

Trp	Leu	Ala	Ser	Gln	Pro	Cys	Met	Tyr	Ser	Leu	Ala	Glu	Trp	Glu	Ser
1					5					10				15	

651

Ala Pro Cys Ser Ala Arg Leu Leu Gly Ile Leu Val Gly Pro Thr Leu
20 25 30

Asn Lys Ser Gln Thr Leu Gly Thr Val Phe Ser Pro Trp Cys Ser Glu
35 40 45

His Leu Trp Glu Arg Leu Leu Ser Val Ser Val Gln Ser Lys Phe Val
50 55 60

Val Xaa Cys Ala Ile Tyr Thr Val Val Gly Trp Arg Lys Val Glu Ser
65 70 75 80

Tyr Thr Gly Lys Lys Leu Pro Ser Phe Asn Phe Ser Val Thr Leu Met
85 90 95

Arg Gly Pro Gln Lys Thr Ser Ser Phe Pro Asn Arg Ile Thr Leu Arg
100 105 110

Arg Thr Gly Leu Gly His Leu Ala Arg Met Ala Pro Ser Cys Cys Cys
115 120 125

Pro Leu Val Arg Asn Leu His Pro Thr Ser Ser Thr Pro Arg Phe Ser
130 135 140

Ser Pro Gln Pro Val Pro Phe Pro Gly Phe Leu Asn Cys Ser Ile Leu
145 150 155 160

Thr Gln Arg Cys Tyr Leu Pro Asn Thr Leu Pro Thr His Ser Cys Gln
165 170 175

Leu Cys Leu Leu Phe Asn Ser Pro His Phe Val Leu Pro Ser Gln Thr
180 185 190

Cys Phe Gln Ser Leu Leu Leu
195

<210> 709

<211> 289

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (49)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (86)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 709

Arg Gly Ser Arg Cys Pro Gly Glu Leu Thr Ser Arg Gly Glu Ala Ser
1 5 10 15

Leu Ser Arg Cys Phe Cys Cys Trp Arg Arg Cys Arg Thr Ala Gly Arg
20 25 30

Lys Gln Cys Gly Pro Trp Ser Trp Pro Thr Ala Cys Arg Ser Ala Thr
35 40 45

Xaa Pro Leu Phe Val Gln His Asp Ala Ala Gln Leu Tyr Leu Lys Leu
50 55 60

Trp Asn Leu Ile Lys Asp Gln Ile Thr Asp Val His Leu Val Glu Arg
65 70 75 80

Leu Gln Ala Leu Tyr Xaa Ile Arg Val Lys Asp Ser Leu Ile Cys Val
85 90 95

Asp Cys Ala Met Glu Ser Ser Arg Asn Ser Ser Met Leu Thr Leu Pro
100 105 110

Leu Ser Leu Phe Asp Val Asp Ser Lys Pro Leu Lys Thr Leu Glu Asp
115 120 125

Ala Leu His Cys Phe Phe Gln Pro Arg Glu Leu Ser Ser Lys Ser Lys
130 135 140

Cys Phe Cys Glu Asn Cys Gly Lys Lys Thr Arg Gly Lys Gln Val Leu
145 150 155 160

Lys Leu Thr His Leu Pro Gln Thr Leu Thr Ile His Leu Met Arg Phe
165 170 175

Ser Ile Arg Asn Ser Gln Thr Arg Lys Ile Cys His Ser Leu Tyr Phe
180 185 190

Pro Gln Ser Leu Asp Phe Ser Gln Ile Leu Pro Met Lys Arg Glu Ser
195 200 205

Cys Asp Ala Glu Glu Gln Ser Gly Gly Gln Tyr Glu Leu Phe Ala Val
210 215 220

Ile Ala His Val Gly Met Ala Asp Ser Gly His Tyr Cys Val Tyr Ile
225 230 235 240

Arg Asn Ala Val Asp Gly Lys Trp Phe Cys Phe Asn Asp Ser Asn Ile
245 250 255

653

Cys Leu Val Ser Trp Glu Asp Ile Gln Cys Thr Tyr Gly Asn Pro Asn
 260 265 270

Tyr His Trp Gln Glu Thr Ala Tyr Leu Leu Val Tyr Met Lys Met Glu
 275 280 285

Cys

<210> 710
 <211> 244
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (189)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (229)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 710
 Pro Ile Pro Thr Lys Leu Pro Leu Thr Lys Ala Glu Glu Lys Ala Leu
 1 5 10 15

Lys Arg Val Arg Arg Lys Ile Lys Asn Lys Ile Ser Ala Gln Glu Ser
 20 25 30

Arg Arg Lys Lys Lys Glu Tyr Val Glu Cys Leu Glu Lys Lys Val Glu
 35 40 45

Thr Phe Thr Ser Glu Asn Asn Glu Leu Trp Lys Lys Val Glu Thr Leu
 50 55 60

Glu Asn Ala Asn Arg Thr Leu Leu Gln Gln Leu Gln Lys Leu Gln Thr
 65 70 75 80

Leu Val Thr Asn Lys Ile Ser Arg Pro Tyr Lys Met Ala Ala Thr Gln
 85 90 95

Thr Gly Thr Cys Leu Met Val Ala Ala Leu Cys Phe Val Leu Val Leu
 100 105 110

Gly Ser Leu Val Pro Cys Leu Pro Glu Phe Ser Ser Gly Ser Gln Thr
 115 120 125

654

Val Lys Glu Asp Pro Leu Ala Ala Asp Gly Val Tyr Thr Ala Ser Gln
 130 135 140
 Met Pro Ser Arg Ser Leu Leu Phe Tyr Asp Asp Gly Ala Gly Leu Trp
 145 150 155 160
 Glu Asp Gly Arg Ser Thr Leu Leu Pro Met Glu Pro Pro Asp Gly Trp
 165 170 175
 Glu Ile Asn Pro Gly Gly Pro Ala Glu Gln Arg Pro Xaa Asp His Leu
 180 185 190
 Gln His Asp His Leu Asp Ser Thr His Glu Thr Thr Lys Tyr Leu Ser
 195 200 205
 Glu Ala Trp Pro Lys Asp Gly Gly Asn Gly Thr Ser Pro Asp Phe Ser
 210 215 220
 His Ser Lys Glu Xaa Phe His Asp Arg Asp Leu Gly Pro Asn Thr Thr
 225 230 235 240
 Ile Lys Leu Ser

<210> 711
 <211> 87
 <212> PRT
 <213> Homo sapiens

<400> 711
 Tyr Thr Cys Ile Thr Glu Ile Pro Ser Tyr Thr Asn Leu Phe Phe Leu
 1 5 10 15
 Leu Leu Asp Arg Asn Val Leu Leu Phe Gln Gln Phe Cys Glu Leu Lys
 20 25 30
 Ser Arg Val Thr Val Gly Leu Glu Trp Leu Val Tyr Leu Gly Met Tyr
 35 40 45
 Tyr Gln Asp Phe Thr Ala Met Leu Gly Asn Asp Arg Glu Asn Asp Arg
 50 55 60
 Asn Glu Ser His Gln Ile Phe Tyr Val Leu Ser Arg Ala Leu Ser Tyr
 65 70 75 80
 Gly Val Tyr Phe Pro Ile Lys
 85

655

<210> 712
<211> 533
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (169)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (495)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 712
Val Asp Pro Arg Val Arg Ser Val Phe Cys Lys Lys Phe Ala Glu Xaa
1 5 10 15
Leu Gly Ser Thr Glu Ala Lys Ala Val Pro Tyr Gln Lys Phe Glu Ala
20 25 30
His Pro Asn Asp Leu Tyr Val Glu Gly Leu Pro Glu Asn Ile Pro Phe
35 40 45
Arg Ser Pro Ser Trp Tyr Gly Ile Pro Arg Leu Glu Lys Ile Ile Gln
50 55 60
Val Gly Asn Arg Ile Lys Phe Val Ile Lys Arg Pro Glu Leu Leu Thr
65 70 75 80
His Ser Thr Thr Glu Val Thr Gln Pro Arg Thr Asn Thr Pro Val Lys
85 90 95
Glu Asp Trp Asn Val Arg Ile Thr Lys Leu Arg Lys Gln Val Glu Glu
100 105 110
Ile Phe Asn Leu Lys Phe Ala Gln Ala Leu Gly Leu Thr Glu Ala Val
115 120 125
Lys Val Pro Tyr Pro Val Phe Glu Ser Asn Pro Glu Phe Leu Tyr Val
130 135 140
Glu Gly Leu Pro Glu Gly Ile Pro Phe Arg Ser Pro Thr Trp Phe Gly
145 150 155 160

656

Ile Pro Arg Leu Glu Arg Ile Val Xaa Gly Ser Asn Lys Ile Lys Phe
165 170 175

Val Val Lys Lys Pro Glu Leu Val Ile Ser Tyr Leu Pro Pro Gly Met
180 185 190

Ala Ser Lys Ile Asn Thr Lys Ala Leu Gln Ser Pro Lys Arg Pro Arg
195 200 205

Ser Pro Gly Ser Asn Ser Lys Val Pro Glu Ile Glu Val Thr Val Glu
210 215 220

Gly Pro Asn Asn Asn Asn Pro Gln Thr Ser Ala Val Arg Thr Pro Thr
225 230 235 240

Gln Thr Asn Gly Ser Asn Val Pro Phe Lys Pro Arg Gly Arg Glu Phe
245 250 255

Ser Phe Glu Ala Trp Asn Ala Lys Ile Thr Asp Leu Lys Gln Lys Val
260 265 270

Glu Asn Leu Phe Asn Glu Lys Cys Gly Glu Ala Leu Gly Leu Lys Gln
275 280 285

Ala Val Lys Val Pro Phe Ala Leu Phe Glu Ser Phe Pro Glu Asp Phe
290 295 300

Tyr Val Glu Gly Leu Pro Glu Gly Val Pro Phe Arg Arg Pro Ser Thr
305 310 315 320

Phe Gly Ile Pro Arg Leu Glu Lys Ile Leu Arg Asn Lys Ala Lys Ile
325 330 335

Lys Phe Ile Ile Lys Lys Pro Glu Met Phe Glu Thr Ala Ile Lys Glu
340 345 350

Ser Thr Ser Ser Lys Ser Pro Pro Arg Lys Ile Asn Ser Ser Pro Asn
355 360 365

Val Asn Thr Thr Ala Ser Gly Val Glu Asp Leu Asn Ile Ile Gln Val
370 375 380

Thr Ile Pro Asp Asp Asp Asn Glu Arg Leu Ser Lys Val Glu Lys Ala
385 390 395 400

Arg Gln Leu Arg Glu Gln Val Asn Asp Leu Phe Ser Arg Lys Phe Gly
405 410 415

Glu Ala Ile Gly Met Gly Phe Pro Val Lys Val Pro Tyr Arg Lys Ile
420 425 430

657

Thr Ile Asn Pro Gly Cys Val Val Val Asp Gly Met Pro Pro Gly Val
 435 440 445

Ser Phe Lys Ala Pro Ser Tyr Leu Glu Ile Ser Ser Met Arg Arg Ile
 450 455 460

Leu Asp Ser Ala Glu Phe Ile Lys Phe Thr Val Ile Arg Pro Phe Pro
 465 470 475 480

Gly Leu Val Ile Asn Asn Gln Leu Val Asp Gln Ser Glu Ser Xaa Gly
 485 490 495

Pro Val Ile Gln Glu Ser Ala Glu Pro Ser Gln Leu Glu Val Pro Ala
 500 505 510

Thr Glu Glu Ile Lys Glu Thr Asp Gly Ser Ser Gln Ile Lys Gln Glu
 515 520 525

Pro Asp Pro Thr Trp
 530

<210> 713

<211> 252

<212> PRT

<213> Homo sapiens

<400> 713

Asn Ser Glu Tyr Cys Tyr Ser Gly Gly Ala Asp Ala Cys Ile His Ser
 1 5 10 15

Trp Lys Ile Pro Asp Leu Ser Met Asp Pro Tyr Asp Gly Tyr Asp Pro
 20 25 30

Ser Val Leu Ser His Val Leu Glu Gly His Gly Asp Ala Val Trp Gly
 35 40 45

Leu Ala Phe Ser Pro Thr Ser Gln Arg Leu Ala Ser Cys Ser Ala Asp
 50 55 60

Gly Thr Val Arg Ile Trp Asp Pro Ser Ser Ser Ser Pro Ala Cys Leu
 65 70 75 80

Cys Thr Phe Pro Thr Ala Ser Glu His Gly Val Pro Thr Ser Val Ala
 85 90 95

Phe Thr Ser Thr Glu Pro Ala His Ile Val Ala Ser Phe Arg Ser Gly
 100 105 110

658

Asp Thr Val Leu Tyr Asp Met Glu Val Gly Ser Ala Leu Leu Thr Leu
 115 120 125
 Glu Ser Arg Gly Ser Ser Gly Pro Thr Gln Ile Asn Gln Val Val Ser
 130 135 140
 His Pro Asn Gln Pro Leu Thr Ile Thr Ala His Asp Asp Arg Gly Ile
 145 150 155 160
 Arg Phe Leu Asp Asn Arg Thr Gly Lys Pro Val His Ser Met Val Ala
 165 170 175
 His Leu Asp Ala Val Thr Cys Leu Ala Val Asp Pro Asn Gly Ala Phe
 180 185 190
 Leu Met Ser Gly Ser His Asp Cys Ser Leu Arg Leu Trp Ser Leu Asp
 195 200 205
 Asn Lys Thr Cys Val Gln Glu Ile Thr Ala His Arg Lys Lys His Glu
 210 215 220
 Glu Ala Ile His Ala Val Ala Cys His Pro Ser Lys Ala Leu Ile Ala
 225 230 235 240
 Ser Ala Gly Ala Asp Ala Leu Ala Lys Val Phe Val
 245 250

<210> 714

<211> 201

<212> PRT

<213> Homo sapiens

<400> 714

Gly His Glu Arg Ser Cys Leu Leu Asn Gly Cys Gly Arg Leu Ala Ala
 1 5 10 15
 Leu Gly Arg Gly Leu Lys Ser Phe Leu Arg Gly Thr Ser Leu Cys Glu
 20 25 30
 Glu Ile Met Ser Leu Ala Leu Arg Ser Glu Leu Val Val Asp Lys Thr
 35 40 45
 Lys Arg Lys Lys Arg Arg Glu Leu Ser Glu Glu Gln Lys Gln Glu Ile
 50 55 60
 Lys Asp Ala Phe Glu Leu Phe Asp Thr Asp Lys Asp Glu Ala Ile Asp
 65 70 75 80
 Tyr His Glu Leu Lys Val Ala Met Arg Ala Leu Gly Phe Asp Val Lys

660

Asp Pro Ser Gly Lys Val His Phe Ala Leu Leu Gly Thr Trp Asp Glu
115 120 125

Lys Met Glu Cys Phe Lys Val Gln Pro Val Ile Gly Glu Asn Gly Gly
130 135 140

Asp Ala Arg Gln Arg Gly His Glu Ala Glu Glu Ser Arg Val Met Leu
145 150 155 160

Trp Lys Arg Asn Pro Leu Pro Lys Asn Ala Glu Asn Met Tyr Tyr Phe
165 170 175

Ser Glu Leu Ala Leu Thr Leu Asn Ala Trp Glu Ser Gly Thr Ala Pro
180 185 190

Thr Asp Ser Arg Leu Arg Pro Asp Gln Arg Leu Met Glu Asn Gly Arg
195 200 205

Trp Asp Glu Ala Asn Ala Glu Lys Gln Arg Leu Glu Glu Lys Gln Arg
210 215 220

Leu Ser Arg Lys Lys Arg Glu Ala Glu Ala Met Lys Ala Thr Glu Asp
225 230 235 240

Gly Thr Pro Tyr Asp Pro Tyr Lys Ala Leu Trp Phe Glu Arg Lys Lys
245 250 255

Asp Pro Val Thr Lys Glu Leu Thr His Ile Tyr Arg Gly Glu Tyr Trp
260 265 270

Glu Cys Lys Glu Lys Gln Asp Trp Ser Ser Cys Pro Asp Ile Phe
275 280 285

<210> 716

<211> 203

<212> PRT

<213> Homo sapiens

<400> 716

Ser Ser Tyr Met Arg Gly Gly Tyr Phe Ser Ser Ser His Glu Gly Phe
1 5 10 15

Ser Tyr Glu Lys Asp Pro Arg Leu Tyr Phe Asp Asp Thr Cys Val Val
20 25 30

Pro Glu Arg Leu Glu Gly Lys Val Lys Gln Glu Pro Thr Met Tyr Arg
35 40 45

661

Glu Gly Pro Pro Tyr Gln Arg Arg Gly Ser Leu Gln Leu Trp Gln Phe
 50 55 60
 Leu Val Thr Leu Leu Asp Asp Pro Ala Asn Ala His Phe Ile Ala Trp
 65 70 75 80
 Thr Gly Arg Gly Met Glu Phe Lys Leu Ile Glu Pro Glu Glu Val Ala
 85 90 95
 Arg Arg Trp Gly Ile Gln Lys Asn Arg Pro Ala Met Asn Tyr Asp Lys
 100 105 110
 Leu Ser Arg Ser Leu Arg Tyr Tyr Tyr Glu Lys Gly Ile Met Gln Lys
 115 120 125
 Val Ala Gly Glu Arg Tyr Val Tyr Lys Phe Val Cys Asp Pro Asp Ala
 130 135 140
 Leu Phe Ser Met Ala Phe Pro Asp Asn Gln Arg Pro Phe Leu Lys Ala
 145 150 155 160
 Glu Ser Glu Cys His Leu Ser Glu Glu Asp Thr Leu Pro Leu Thr His
 165 170 175
 Phe Glu Asp Ser Pro Ala Tyr Leu Leu Asp Met Asp Arg Cys Ser Ser
 180 185 190
 Leu Pro Tyr Ala Glu Val Cys Leu Leu Ser Phe
 195 200

<210> 717

<211> 88

<212> PRT

<213> Homo sapiens

<400> 717

Ile Ile Gly Lys Glu Asp Asn Ser Glu Lys Pro Asn Ile Thr Lys Gly
 1 5 10 15
 Gly Leu Ala Leu Leu Glu Lys Tyr Thr Lys Leu Val Tyr Tyr Asn Thr
 20 25 30
 Trp Leu Tyr Val Gly Asn Val Thr Thr Gly Gln Ile His Leu Leu Cys
 35 40 45
 Ser Arg Gly Ser Pro Phe Leu Cys Arg Lys Tyr Asn Thr His Cys Met
 50 55 60
 Arg Ser Leu Arg Val Asp Ser Asn Pro Gly Leu Ser Thr Leu Asp Ile

662

65 70 75 80

Met His Val Gly Arg Trp Val Trp

85

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<210> 718
<211> 359
<212> PRT
<213> Homo sapiens
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<400> 718
Gly Leu Glu Tyr Pro Met Leu His Tyr Val Gly Phe Val Pro Val Ile
1 5 10 15

Asp Gly Asp Phe Ile Pro Ala Asp Pro Ile Asn Leu Tyr Ala Asn Ala
20 25 30

Ala Asp Ile Asp Tyr Ile Ala Gly Thr Asn Asn Met Asp Gly His Ile
35 40 45

Phe Ala Ser Ile Asp Met Pro Ala Ile Asn Lys Gly Asn Lys Lys Val
50 55 60

Thr	Glu	Glu	Asp	Phe	Tyr	Lys	Leu	Val	Ser	Glu	Phe	Thr	Ile	Thr	Lys
65					70					75					80

Gly Leu Arg Gly Ala Lys Thr Thr Phe Asp Val Tyr Thr Glu Ser Trp
85 90 95

Ala Gln Asp Pro Ser Gln Glu Asn Lys Lys Lys Thr Val Val Asp Phe
100 105 110

Glu Thr Asp Val Leu Phe Leu Val Pro Thr Glu Ile Ala Leu Ala Gln
115 120 125

His Arg Ala Asn Ala Lys Ser Ala Lys Thr Tyr Ala Tyr Leu Phe Ser
130 135 140

```
His Pro Ser Arg Met Pro Val Tyr Pro Lys Trp Val Gly Ala Asp His
145                      150                      155                      160
```

Ala Asp Asp Ile Gln Tyr Val Phe Gly Lys Pro Phe Ala Thr Pro Thr
165 170 175

Gly Tyr Arg Pro Gln Asp Arg Thr Val Ser Lys Ala Met Ile Ala Tyr
180 185 190

Trp Thr Asn Phe Ala Lys Thr Gly Asp Pro Asn Met Gly Asp Ser Ala
195 200 205

Val Pro Thr His Trp Glu Pro Tyr Thr Thr Glu Asn Ser Gly Tyr Leu
 210 215 220
 Glu Ile Thr Lys Lys Met Gly Ser Ser Ser Met Lys Arg Ser Leu Arg
 225 230 235 240
 Thr Asn Phe Leu Arg Tyr Trp Thr Leu Thr Tyr Leu Ala Leu Pro Thr
 245 250 255
 Val Thr Asp Gln Glu Ala Thr Pro Val Pro Pro Thr Gly Asp Ser Glu
 260 265 270
 Ala Thr Pro Val Pro Pro Thr Gly Asp Ser Glu Thr Ala Pro Val Pro
 275 280 285
 Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser
 290 295 300
 Gly Ala Pro Pro Val Thr Pro Thr Gly Asp Ser Glu Thr Ala Pro Val
 305 310 315 320
 Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp
 325 330 335
 Ser Glu Ala Ala Pro Val Pro Pro Thr Asp Asp Ser Lys Glu Ala Gln
 340 345 350
 Met Pro Ala Val Ile Arg Phe
 355

<210> 719
 <211> 134
 <212> PRT
 <213> Homo sapiens

<400> 719
 Ser Ser Pro Leu Arg Pro Leu Leu Leu Ala Leu Ala Leu Ala Ser Val
 1 5 10 15
 Pro Cys Ala Gln Gly Ala Cys Pro Ala Ser Ala Asp Leu Lys His Ser
 20 25 30
 Asp Gly Thr Arg Thr Cys Ala Lys Leu Tyr Asp Lys Ser Asp Pro Tyr
 35 40 45
 Tyr Glu Asn Cys Cys Gly Gly Ala Glu Leu Ser Leu Glu Ser Gly Ala
 50 55 60

664

Asp Leu Pro Tyr Leu Pro Ser Asn Trp Ala Asn Thr Ala Ser Ser Leu
65 70 75 80

Val Val Ala Pro Arg Cys Glu Leu Thr Val Trp Ser Arg Gln Gly Lys
85 90 95

Ala Gly Lys Thr His Lys Phe Ser Ala Gly Thr Tyr Pro Arg Leu Glu
100 105 110

Glu Tyr Arg Arg Gly Ile Leu Gly Asp Trp Ser Asn Ala Ile Ser Ala
115 120 125

Leu Tyr Cys Arg Cys Ser
130

<210> 720

<211> 47

<212> PRT

<213> Homo sapiens

<400> 720

Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Gly Gly Arg Ser Arg Gly
1 5 10 15

Ser Lys Leu Thr Tyr Ala Cys Met Arg Arg His Ser Ser Ser Ile Val
20 25 30

Ser Pro Lys Phe Asn Ser Leu Ala Val Val Leu Gln Arg Arg Asp
35 40 45

<210> 721

<211> 122

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (114)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 721

Lys Leu Phe Leu Leu Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
1 5 10 15

Gly Gly Arg Ser Arg Gly Ser Lys Leu Thr Tyr Ala Cys Met Arg Arg
20 25 30

665

His Ser Ser Ser Ile Val Ser Pro Lys Phe Asn Ser Leu Ala Val Val
35 40 45

Leu Gln Arg Arg Asp Trp Glu Asn Pro Gly Val Thr Gln Leu Asn Arg
50 55 60

Leu Ala Ala His Pro Pro Phe Ala Ser Trp Arg Asn Ser Glu Glu Ala
65 70 75 80

Arg Thr Asp Arg Pro Ser Gln Gln Leu Arg Ser Leu Asn Gly Glu Trp
85 90 95

Asp Ala Pro Cys Ser Gly Ala Leu Ser Ala Ala Gly Val Val Val Thr
100 105 110

Arg Xaa Val Thr Ala Thr Leu Ala Ser Ala
115 120

<210> 722

<211> 100

<212> PRT

<213> Homo sapiens

<400> 722

Ser Thr Ala Pro Thr Pro Val Met Asp Asn Ser Arg Asn Ala Pro Leu
1 5 10 15

Ala Gly Phe Gly Tyr Gly Leu Pro Ile Ser Arg Leu Tyr Ala Lys Tyr
20 25 30

Phe Gln Gly Asp Leu Asn Leu Tyr Ser Leu Ser Gly Tyr Gly Thr Asp
35 40 45

Ala Ile Ile Tyr Leu Lys Ala Leu Ser Ser Glu Ser Ile Glu Lys Leu
50 55 60

Pro Val Phe Asn Lys Ser Ala Phe Lys His Tyr Gln Met Ser Ser Glu
65 70 75 80

Ala Asp Asp Trp Cys Ile Pro Ser Arg Glu Pro Lys Asn Leu Ala Lys
85 90 95

Glu Val Ala Met
100

<210> 723

<211> 372

666

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (199)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 723

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Arg Gln His Lys Ile Ser Glu Thr Leu Glu Ser Arg His His Lys Ile
 1              5              10              15

Lys Thr Gly Ser Pro Gly Ser Glu Val Val Thr Leu Gln Gln Phe Leu
      20              25              30

Glu Glu Ser Asn Lys Leu Thr Ser Val Gln Ile Lys Ser Ser Ser Gln
      35              40              45

Glu Asn Leu Leu Asp Glu Val Met Lys Ser Leu Ser Val Ser Ser Asp
      50              55              60

Phe Leu Gly Lys Asp Lys Pro Val Ser Cys Gly Leu Ala Arg Ser Val
      65              70              75              80

Ser Gly Lys Thr Pro Gly Asp Phe Tyr Asp Arg Arg Thr Thr Lys Pro
      85              90              95

Glu Phe Leu Arg Pro Gly Pro Arg Lys Thr Glu Asp Thr Tyr Phe Ile
      100              105              110

Ser Ser Ala Gly Lys Pro Thr Pro Gly Thr Gln Gly Lys Ile Lys Leu
      115              120              125

Val Lys Glu Ser Ser Leu Ser Arg Gln Ser Lys Asp Ser Asn Pro Tyr
      130              135              140

Ala Thr Leu Pro Arg Ala Ser Ser Val Ile Ser Thr Ala Glu Gly Thr
      145              150              155              160

Thr Arg Arg Thr Ser Ile His Asp Phe Leu Thr Lys Asp Ser Arg Leu
      165              170              175

Pro Ile Ser Val Asp Ser Pro Pro Ala Ala Ala Asp Ser Asn Thr Thr
      180              185              190

Ala Ala Ser Ser Glu Tyr Xaa Leu His Gln Trp Ser Ser His Ile Leu
      195              200              205

Asp Ile Pro Thr His Thr Ile Gly Ser Cys Ala Gln Asn Asp Leu Ala
      210              215              220

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<220>
<221> SITE
<222> (2)
<223> Xaa equals any of the naturally occurring L-amino acids
```

Gln Ile Ser Asn Lys Leu Leu Lys Thr Gln Arg Phe Gly Leu Leu Phe
35 40 45

668

Leu Ser Leu Ala Val Arg His Gly Val Ser Gly Arg Arg Asn Arg Arg
 50 55 60

Gly Asn Leu His Gly Asp Ser Tyr
 65 70

<210> 725

<211> 73

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (48)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 725

Ala Ser Ile Asn Phe Tyr Phe Leu Trp Val Leu Leu Lys Asp Leu Asn
 1 5 10 15

Met Glu Lys Ser Cys His Gly Ser Glu Leu His Asn Ala Leu Asn Arg
 20 25 30

Arg Pro Ser Ile Phe Phe Thr Leu Ser Thr Leu Ala Ala Phe Cys Xaa
 35 40 45

Phe Tyr Gln Asn Gly Leu Phe Leu Gly Lys Leu Phe Pro Pro Phe Trp
 50 55 60

Met Gly Arg Gly Phe Pro Gln Trp Phe
 65 70

<210> 726

<211> 406

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (160)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 726

Arg Phe Val Phe Ser Ser Glu Leu His Gly Lys Ser Ala Tyr Ser Lys
 1 5 10 15

669

Val Thr Cys Met Pro His Leu Met Glu Arg Met Val Gly Ser Gly Leu
 20 25 30

Leu Trp Leu Ala Leu Val Ser Cys Ile Leu Thr Gln Ala Ser Ala Val
 35 40 45

Gln Arg Asp Pro Ser Thr Val Glu Asp Lys Cys Glu Lys Ala Cys Arg
 50 55 60

Pro Glu Glu Glu Cys Leu Ala Leu Asn Ser Thr Trp Gly Cys Phe Cys
 65 70 75 80

Arg Gln Asp Leu Asn Ser Ser Asp Val His Ser Leu Gln Pro Gln Leu
 85 90 95

Asp Cys Gly Pro Arg Glu Ile Lys Val Lys Val Asp Lys Cys Leu Leu
 100 105 110

Gly Gly Leu Gly Leu Gly Glu Glu Val Ile Ala Tyr Leu Arg Asp Pro
 115 120 125

Asn Cys Ser Ser Ile Leu Gln Thr Glu Glu Arg Asn Trp Val Ser Val
 130 135 140

Thr Ser Pro Val Gln Ala Ser Ala Cys Arg Asn Ile Leu Glu Arg Xaa
 145 150 155 160

Gln Thr His Ala Ile Tyr Lys Asn Thr Leu Ser Leu Val Asn Asp Phe
 165 170 175

Ile Ile Arg Asp Thr Ile Leu Asn Ile Asn Phe Gln Cys Ala Tyr Pro
 180 185 190

Leu Asp Met Lys Val Ser Leu Gln Ala Ala Leu Gln Pro Ile Val Ser
 195 200 205

Ser Leu Asn Val Ser Val Asp Gly Asn Gly Glu Phe Ile Val Arg Met
 210 215 220

Ala Leu Phe Gln Asp Gln Asn Tyr Thr Asn Pro Tyr Glu Gly Asp Ala
 225 230 235 240

Val Glu Leu Ser Val Glu Ser Val Leu Tyr Val Gly Ala Ile Leu Glu
 245 250 255

Gln Gly Asp Thr Ser Arg Phe Asn Leu Val Leu Arg Asn Cys Tyr Ala
 260 265 270

Thr Pro Thr Glu Asp Lys Ala Asp Leu Val Lys Tyr Phe Ile Ile Arg
 275 280 285

670

Asn Ser Cys Ser Asn Gln Arg Asp Ser Thr Ile His Val Glu Glu Asn
 290 295 300
 Gly Gln Ser Ser Glu Ser Arg Phe Ser Val Gln Met Phe Met Phe Ala
 305 310 315 320
 Gly His Tyr Asp Leu Val Phe Leu His Cys Glu Ile His Leu Cys Asp
 325 330 335
 Ser Leu Asn Glu Gln Cys Gln Pro Ser Cys Ser Arg Ser Gln Val Arg
 340 345 350
 Ser Glu Val Pro Ala Ile Asp Leu Ala Arg Val Leu Asp Leu Gly Pro
 355 360 365
 Ile Thr Arg Arg Gly Ala Gln Ser Pro Gly Val Met Asn Gly Thr Pro
 370 375 380
 Ser Thr Ala Gly Phe Leu Val Ala Trp Pro Met Val Leu Leu Thr Val
 385 390 395 400
 Leu Leu Ala Trp Leu Phe
 405

<210> 727

<211> 159

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (144)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 727

Gln His Ile Pro Tyr Arg Glu Asp Lys Asn Leu Thr Gly Thr Ala Arg
 1 5 10 15
 Tyr Ala Ser Ile Asn Ala His Leu Gly Ile Glu Gln Ser Arg Arg Asp
 20 25 30
 Asp Met Glu Ser Leu Gly Tyr Val Leu Met Tyr Phe Asn Arg Thr Ser
 35 40 45
 Leu Pro Trp Gln Gly Leu Lys Ala Ala Thr Lys Lys Gln Lys Tyr Glu
 50 55 60
 Lys Ile Ser Glu Lys Lys Met Ser Thr Pro Val Glu Val Leu Cys Lys
 65 70 75 80

671

Gly Phe Pro Ala Glu Phe Ala Met Tyr Leu Asn Tyr Cys Arg Gly Leu
 85 90 95
 Arg Phe Glu Glu Ala Pro Asp Tyr Met Tyr Leu Arg Gln Leu Phe Arg
 100 105 110
 Ile Leu Phe Arg Thr Leu Asn His Gln Tyr Asp Tyr Thr Phe Asp Trp
 115 120 125
 Thr Met Leu Lys Gln Lys Ala Ala Gln Gln Ala Ala Ser Ser Ser Xaa
 130 135 140
 Ala Gly Ser Ala Gly Pro Asn Pro His Arg Phe Leu Ser Met Asn
 145 150 155

<210> 728

<211> 226

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (4)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (15)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (108)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 728

Glu Pro Leu Xaa Pro Ala Gly Thr Gln Arg Val Cys Leu Val Xaa Pro
 1 5 10 15
 Asp Val Lys Trp Gly Pro Gly Lys Ser Gln Met Thr Arg Ala Glu Trp
 20 25 30
 Gln Val Ala Glu Ala Lys Thr Leu Val His Thr Leu Asp Gly Trp Ser
 35 40 45
 Val Val Gln Thr Met Val Val Ser Thr Lys Thr Pro Asp Arg Lys Leu
 50 55 60

672

Ile Phe Gly Lys Gly Asn Phe Glu His Leu Thr Glu Lys Ile Arg Gly
65 70 75 80

Ser Pro Asp Val Thr Cys Val Phe Leu Asn Val Glu Arg Met Ala Ala
85 90 95

Pro Thr Lys Lys Glu Leu Glu Ala Ala Trp Gly Xaa Glu Val Phe Asp
100 105 110

Arg Phe Thr Val Val Leu His Ile Phe Arg Cys Asn Ala Arg Thr Lys
115 120 125

Glu Ala Arg Leu Gln Val Ala Leu Ala Glu Met Pro Leu His Arg Ser
130 135 140

Asn Leu Lys Arg Asp Val Ala His Leu Tyr Arg Gly Val Gly Ser Arg
145 150 155 160

Tyr Ile Met Gly Ser Gly Glu Ser Phe Met Gln Leu Gln Gln Arg Leu
165 170 175

Leu Arg Glu Lys Glu Ala Lys Ile Arg Lys Ala Leu Asp Arg Leu Arg
180 185 190

Lys Lys Arg His Leu Leu Arg Arg Gln Arg Arg Arg Arg Glu Phe Pro
195 200 205

Val Ile Ser Val Val Gly Tyr Thr Asn Leu Arg Lys Asp His Val Ile
210 215 220

Lys Asp
225

<210> 729

<211> 61

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (39)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (54)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 729

673

Leu Cys Leu Gln Gly Tyr Tyr Arg Gly Ala Val Gly Ala Leu Leu Val
 1 5 10 15

Phe Asp Leu Thr Lys His Gln Thr Tyr Ala Val Val Glu Arg Trp Leu
 20 25 30

Lys Glu Leu Tyr Asp His Xaa Glu Ala Thr Ile Val Val Met Leu Val
 35 40 45

Gly Asn Lys Met Thr Xaa Ala Arg Pro Gly Lys Cys Pro
 50 55 60

<210> 730

<211> 272

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (263)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 730

Pro Phe His Gln Gly Phe Arg Leu Leu Pro Ala Ala Trp Thr Pro Ala
 1 5 10 15

Thr Gly Ser Pro Ser Gln Ser Ser Ile Lys Ala Trp Arg Thr Pro Cys
 20 25 30

Leu Ser Val Pro Gly Lys Lys Lys Asn Gln Trp Phe Glu Arg Gln Val
 35 40 45

Arg Trp Ser Thr Ala Thr Ser Val Thr Cys Cys Ser Ser Cys Thr Val
 50 55 60

Ser Met Pro Pro Ser Pro Arg Ser Val Gly Trp Ser Gly Lys Arg Arg
 65 70 75 80

Leu Arg Ile Leu Pro Ala Ser Pro Ser Ser Gly Ser Ala Ser Gly Trp
 85 90 95

Thr Ile Arg Thr Ser Thr Ala Leu Gly Ile Ser Ser Val Ile Thr Ala
 100 105 110

Trp Gly Val Leu Phe Asn Asp Ser Thr Arg Leu Ile Leu Tyr Asn Asp
 115 120 125

Gly Asp Ser Leu Gln Tyr Ile Glu Arg Asp Gly Thr Glu Ser Tyr Leu
 130 135 140

674

Thr Val Ser Ser His Pro Asn Ser Leu Met Lys Lys Ile Thr Leu Leu
145 150 155 160

Lys Tyr Phe Arg Asn Tyr Met Ser Glu His Leu Leu Lys Ala Gly Ala
 165 170 175

Asn Ile Thr Pro Arg Glu Gly Asp Glu Leu Ala Arg Leu Pro Tyr Leu
 180 185 190

Arg Thr Trp Phe Arg Thr Arg Ser Ala Ile Ile Leu His Leu Ser Asn
 195 200 205

Gly Ser Val Gln Ile Asn Phe Phe Gln Asp His Thr Lys Leu Ile Leu
 210 215 220

Cys Pro Leu Met Ala Ala Val Thr Tyr Ile Asp Glu Lys Arg Asp Phe
225 230 235 240

Arg Thr Tyr Arg Leu Ser Leu Leu Glu Glu Tyr Gly Cys Cys Lys Glu
 245 250 255

Leu Ala Ser Arg Leu Arg Xaa Arg Pro His Tyr Gly Gly Gln Ala Ala
 260 265 270

<210> 731

<211> 175

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (137)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (167)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (168)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

675

<221> SITE

<222> (169)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 731

Leu Ser Cys Cys Arg Arg Arg Leu Cys Arg Arg Arg Glu Cys Gly Val
1 5 10 15

Gly Thr Gly Ala Ala Ala Ala Thr Pro Gly Ile Phe Val Ala Ser
20 25 30

Ser Arg Pro Phe Cys Pro Ala Ala Phe Pro Gln Ser Ala Leu Pro Thr
35 40 45

Pro Leu Arg Pro Gly Ala Pro Ala Ser Ile Ser Arg Ser Leu Ser Thr
50 55 60

Thr His Thr Ala Pro Pro Ile Met Asp Pro Gly Ser Gly Gly Gly Gly
65 70 75 80

Gly Gly Gly Gly Gly Gly Gly Ser Ser Ser Gly Ser Ser Ser Ser Asp
85 90 95

Ser Ala Pro Asp Cys Trp Asp Gln Ala Asp Met Glu Ala Pro Gly Pro
100 105 110

Gly Pro Cys Gly Gly Gly Gly Ser Leu Ala Ala Ala Glu Ala Gln
115 120 125

Arg Glu Asn Leu Ser Ala Ala Phe Xaa Arg Gln Leu Asn Val Asn Ala
130 135 140

Lys Pro Phe Val Pro Asn Val His Ala Ala Glu Phe Val Pro Ser Phe
145 150 155 160

Leu Arg Gly Pro Ala Ala Xaa Xaa Xaa Pro Ala Gly Gly Gly Arg
165 170 175

<210> 732

<211> 133

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (81)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

676

<221> SITE
 <222> (122)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (129)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (130)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 732
 Thr Leu Gly Pro Asp Cys Ser Glu Leu Ala Ala Val Leu Leu Arg Met
 1 5 10 15
 Asp Gly Arg Leu Asp Gly Trp Val Asp Gly Arg Gly Trp Pro Trp Met
 20 25 30
 Arg Ser Ala Leu His Thr Gln Thr Arg Trp Glu Arg Phe Val Glu His
 35 40 45
 Asp Ser Leu Gln Gln Glu Tyr Met Cys Ala Tyr Leu Cys Gly Gln Lys
 50 55 60
 Tyr Leu His Leu Gly Phe Gly Ala Ile Gln Glu Glu Met Ser Gln Lys
 65 70 75 80
 Xaa Leu Asn Gln Gly Leu Ser Thr Leu Trp Ile Leu Asn Leu Lys Met
 85 90 95
 Gly Ala Gly Leu Cys Leu Lys Ala Leu Leu Ser His Leu Leu Gly Pro
 100 105 110
 Trp Phe Asn Lys Ala Leu Ser Lys Leu Xaa Lys Lys Lys Lys Lys Lys
 115 120 125
 Xaa Xaa Lys Lys Arg
 130

<210> 733
 <211> 61
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE

677

<222> (46)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 733

His Tyr Asn Lys Arg Ser Thr Ile Thr Ser Arg Glu Ile Gln Thr Ala
1 5 10 15

Val Arg Leu Leu Leu Pro Gly Glu Leu Ala Lys His Ala Val Ser Glu
20 25 30

Gly Thr Lys Ala Val Thr Gln Val His Pro Ala Pro Lys Xaa Glu Leu
35 40 45

Pro Gly Pro Gly Ala Arg Ser Leu Glu Ser Pro Ala Ala
50 55 60

<210> 734

<211> 106

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (36)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 734

Gly Ser Asp Gly Pro Arg Glu Arg Ala Pro Val Ala Trp Leu Ser His
1 5 10 15

Ser Ile Leu Ser Leu Ile Leu Asn Lys Tyr Phe Leu Trp Gly Phe Phe
20 25 30

Phe Phe Leu Xaa Ala Val Val Cys Phe Lys Leu Thr Thr Trp Lys Lys
35 40 45

His Leu Gly Tyr Leu Trp Phe Ser Cys Leu Val Pro Ala Ser Thr Pro
50 55 60

Thr Pro Phe Glu Ser Gly Asp Ser Phe Phe Cys Val Glu Thr Arg Trp
65 70 75 80

Pro Arg Gln Glu Val Lys Ala Ala Ile Arg Lys Ala Leu Gly Thr Leu
85 90 95

Val Pro Val Ala Arg Leu Gln Val Thr Ser
100 105

678

<210> 735

<211> 349

<212> PRT

<213> Homo sapiens

<400> 735

Ala Arg Gly Pro Gly Gly Ala Asp Ser Ser Lys Pro Arg Ile Leu Leu
 1 5 10 15

Met Gly Leu Arg Arg Ser Gly Lys Ser Ser Ile Gln Lys Val Val Phe
 20 25 30

His Lys Met Ser Pro Asn Glu Thr Leu Phe Leu Glu Ser Thr Asn Lys
 35 40 45

Ile Tyr Lys Asp Asp Ile Ser Asn Ser Ser Phe Val Asn Phe Gln Ile
 50 55 60

Trp Asp Phe Pro Gly Gln Met Asp Phe Phe Asp Pro Thr Phe Asp Tyr
 65 70 75 80

Glu Met Ile Phe Arg Gly Thr Gly Ala Leu Ile Tyr Val Ile Asp Ala
 85 90 95

Gln Asp Asp Tyr Met Glu Ala Leu Thr Arg Leu His Ile Thr Val Ser
 100 105 110

Lys Ala Tyr Lys Val Asn Pro Asp Met Asn Phe Glu Val Phe Ile His
 115 120 125

Lys Val Asp Gly Leu Ser Asp Asp His Lys Ile Glu Thr Gln Arg Asp
 130 135 140

Ile His Gln Arg Ala Asn Asp Asp Leu Ala Asp Ala Gly Leu Glu Lys
 145 150 155 160

Leu His Leu Ser Phe Tyr Leu Thr Ser Ile Tyr Asp His Ser Ile Phe
 165 170 175

Glu Ala Phe Ser Lys Val Val Gln Lys Leu Ile Pro Gln Leu Pro Thr
 180 185 190

Leu Glu Asn Leu Leu Asn Ile Phe Ile Ser Asn Ser Gly Ile Glu Lys
 195 200 205

Ala Phe Leu Phe Asp Val Val Ser Lys Ile Tyr Ile Ala Thr Asp Ser
 210 215 220

Ser Pro Val Asp Met Gln Ser Tyr Glu Leu Cys Cys Asp Met Ile Asp
 225 230 235 240

679

Val Val Ile Asp Val Ser Cys Ile Tyr Gly Leu Lys Glu Asp Gly Ser
 245 250 255
 Gly Ser Ala Tyr Asp Lys Glu Ser Met Ala Ile Ile Lys Leu Asn Asn
 260 265 270
 Thr Thr Val Leu Tyr Leu Lys Glu Val Thr Lys Phe Leu Ala Leu Val
 275 280 285
 Cys Ile Leu Arg Glu Glu Ser Phe Glu Arg Lys Gly Leu Ile Asp Tyr
 290 295 300
 Asn Phe His Cys Phe Arg Lys Ala Ile His Glu Val Phe Glu Val Gly
 305 310 315 320
 Val Thr Ser His Arg Ser Cys Gly His Gln Thr Ser Ala Ser Ser Leu
 325 330 335
 Lys Ala Leu Thr His Asn Gly Thr Pro Arg Asn Ala Ile
 340 345

<210> 736

<211> 468

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (250)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (301)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (306)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 736

Ala Ala Cys Cys Phe Ser Cys Trp Ala Ser Ser Gly Phe Ala Phe Val
 1 5 10 15

Ala Ser Glu Pro Leu Ala Phe Lys Pro Leu Ser Leu Leu Leu Pro His
 20 25 30

680

Thr Pro Leu Ser Leu Thr Pro Leu Phe Cys Cys Pro Val Thr Cys Pro
 35 40 45
 Lys Leu Cys Pro Glu Leu Arg Thr Phe Pro Phe Leu Ser Leu Glu Pro
 50 55 60
 Phe Phe Asp Ser Thr Lys Pro Ser Trp Tyr Pro Gly Met Thr Arg Leu
 65 70 75 80
 Leu Asp Ala Glu Trp Trp Arg Arg Ser Glu Ala Gly His Leu Arg Arg
 85 90 95
 Gln Val Ala Ala Val Leu Phe Phe Pro Glu Gly Thr Cys Ser Asn Lys
 100 105 110
 Lys Ala Leu Leu Lys Phe Lys Pro Gly Ala Phe Ile Ala Gly Val Pro
 115 120 125
 Val Gln Pro Val Leu Ile Arg Tyr Pro Asn Ser Leu Asp Thr Thr Ser
 130 135 140
 Trp Ala Trp Arg Gly Pro Gly Val Leu Lys Val Leu Trp Leu Thr Ala
 145 150 155 160
 Ser Gln Pro Cys Ser Ile Val Asp Val Glu Phe Leu Pro Val Tyr His
 165 170 175
 Pro Ser Pro Glu Glu Ser Arg Asp Pro Thr Leu Tyr Ala Asn Asn Val
 180 185 190
 Gln Arg Val Met Ala Gln Ala Leu Gly Ile Pro Ala Thr Glu Cys Glu
 195 200 205
 Phe Val Gly Ser Leu Pro Val Ile Val Val Gly Arg Leu Lys Val Ala
 210 215 220
 Leu Glu Pro Gln Leu Trp Glu Leu Gly Lys Val Leu Arg Lys Ala Gly
 225 230 235 240
 Leu Ser Ala Gly Tyr Val Asp Ala Gly Xaa Glu Pro Gly Arg Ser Arg
 245 250 255
 Met Ile Ser Gln Glu Glu Phe Ala Arg Gln Leu Gln Leu Ser Asp Pro
 260 265 270
 Gln Thr Val Ala Gly Ala Phe Gly Tyr Phe Gln Gln Asp Thr Lys Gly
 275 280 285
 Leu Val Asp Phe Arg Asp Val Ala Leu Ala Leu Xaa Leu Asp Gly
 290 295 300

681

Gly Xaa Ser Leu Glu Glu Leu Thr Arg Leu Ala Phe Glu Leu Phe Ala
 305 310 315 320

Glu Glu Gln Ala Glu Gly Pro Asn Arg Leu Leu Tyr Lys Asp Gly Phe
 325 330 335

Ser Thr Ile Leu His Leu Leu Leu Gly Ser Pro His Pro Ala Ala Thr
 340 345 350

Ala Leu His Ala Glu Leu Cys Gln Ala Gly Ser Ser Gln Gly Leu Ser
 355 360 365

Leu Cys Gln Phe Gln Asn Phe Ser Leu His Asp Pro Leu Tyr Gly Lys
 370 375 380

Leu Phe Ser Thr Tyr Leu Arg Pro Pro His Thr Ser Arg Gly Thr Ser
 385 390 395 400

Gln Thr Pro Asn Ala Ser Ser Pro Gly Asn Pro Thr Ala Leu Ala Asn
 405 410 415

Gly Thr Gly Lys His Pro Ser Arg Arg Glu Thr Glu Cys Leu Ser Leu
 420 425 430

Ser Pro Pro Pro Pro Gln Gly Ser Ala Arg Gly Leu Pro Tyr Ala Ser
 435 440 445

Ala Pro Ser Leu Leu Leu Phe Glu Phe Cys Tyr Cys Cys Leu Val Val
 450 455 460

Val Phe Leu Ser
 465

<210> 737

<211> 184

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (24)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 737

Arg Glu Ser Pro Phe Pro Leu Pro Ser Gly Arg Glu Glu Arg Arg Gly
 1 5 10 15

Gln Gly Lys Lys Leu Leu Val Xaa Leu Thr Met Lys Thr Leu Leu
 20 25 30

Leu Leu Leu Val Leu Leu Glu Leu Gly Glu Ala Gln Gly Ser Leu His
35 40 45

Arg Val Pro Leu Arg Arg His Pro Ser Leu Lys Lys Lys Leu Arg Ala
50 55 60

Arg Ser Gln Leu Ser Glu Phe Trp Lys Ser His Asn Leu Asp Met Ile
65 70 75 80

Gln Phe Thr Glu Ser Cys Ser Met Asp Gln Ser Ala Lys Glu Pro Leu
85 90 95

Ile Asn Tyr Leu Asp Met Glu Tyr Phe Gly Thr Ile Ser Ile Gly Ser
100 105 110

Pro Pro Gln Asn Phe Thr Val Ile Phe Asp Thr Gly Ser Ser Asn Leu
115 120 125

Trp Val Pro Ser Val Tyr Cys Thr Ser Pro Ala Cys Lys Thr His Ser
130 135 140

Arg Phe Gln Pro Ser Gln Ser Ser Thr Tyr Ser Gln Pro Gly Gln Ser
145 150 155 160

Phe Ser Ile Gln Tyr Gly Thr Gly Ser Leu Ser Gly Ile Ile Gly Ser
165 170 175

Arg Pro Ser Leu Cys Gly Lys Asp
180

<210> 738

<211> 624

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (2)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (188)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (192)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 738

His Xaa His Ser Phe Ser Ser Gly Tyr Val Glu Met Glu Phe Glu Phe
1 5 10 15

Asp Arg Leu Arg Ala Phe Gln Ala Met Gln Val His Cys Asn Asn Met
20 25 30

His Thr Leu Gly Ala Arg Leu Pro Gly Gly Val Glu Cys Arg Phe Arg
35 40 45

Arg Gly Pro Ala Met Ala Trp Glu Gly Glu Pro Met Arg His Asn Leu
50 55 60

Gly Gly Asn Leu Gly Asp Pro Arg Ala Arg Ala Val Ser Val Pro Leu
65 70 75 80

Gly Gly Arg Val Ala Arg Phe Leu Gln Cys Arg Phe Leu Phe Ala Gly
85 90 95

Pro Trp Leu Leu Phe Ser Glu Ile Ser Phe Ile Ser Asp Val Val Asn
100 105 110

Asn Ser Ser Pro Ala Leu Gly Gly Thr Phe Pro Pro Ala Pro Trp Trp
115 120 125

Pro Pro Gly Pro Pro Pro Thr Asn Phe Ser Ser Leu Glu Leu Glu Pro
130 135 140

Arg Gly Gln Gln Pro Val Ala Lys Ala Glu Gly Ser Pro Thr Ala Ile
145 150 155 160

Leu Ile Gly Cys Leu Val Ala Ile Ile Leu Leu Leu Leu Ile Ile
165 170 175

Ala Leu Met Leu Trp Arg Leu His Trp Arg Arg Xaa Leu Ser Lys Xaa
180 185 190

Glu Arg Arg Val Leu Glu Glu Glu Leu Thr Val His Leu Ser Val Pro
195 200 205

Gly Asp Thr Ile Leu Ile Asn Asn Arg Pro Gly Pro Arg Glu Pro Pro
210 215 220

Pro Tyr Gln Glu Pro Arg Pro Arg Gly Asn Pro Pro His Ser Ala Pro
225 230 235 240

Cys Val Pro Asn Gly Ser Ala Leu Leu Leu Ser Asn Pro Ala Tyr Arg
245 250 255

Leu Leu Leu Ala Thr Tyr Ala Arg Pro Pro Arg Gly Pro Gly Pro Pro
 260 265 270

Thr Pro Ala Trp Ala Lys Pro Thr Asn Thr Gln Ala Tyr Ser Gly Asp
 275 280 285

Tyr Met Glu Pro Glu Lys Pro Gly Ala Pro Leu Leu Pro Pro Pro Pro
 290 295 300

Gln Asn Ser Val Pro His Tyr Ala Glu Ala Asp Ile Val Thr Leu Gln
 305 310 315 320

Gly Val Thr Gly Gly Asn Thr Tyr Ala Val Pro Ala Leu Pro Pro Gly
 325 330 335

Ala Val Gly Asp Gly Pro Pro Arg Val Asp Phe Pro Arg Ser Arg Leu
 340 345 350

Arg Phe Lys Glu Lys Leu Gly Glu Gly Gln Phe Gly Glu Val His Leu
 355 360 365

Cys Glu Val Asp Ser Pro Gln Asp Leu Val Ser Leu Asp Phe Pro Leu
 370 375 380

Asn Val Arg Lys Gly His Pro Leu Leu Val Ala Val Lys Ile Leu Arg
 385 390 395 400

Pro Asp Ala Thr Lys Asn Ala Arg Asn Asp Phe Leu Lys Glu Val Lys
 405 410 415

Ile Met Ser Arg Leu Lys Asp Pro Asn Ile Ile Arg Leu Leu Gly Val
 420 425 430

Cys Val Gln Asp Asp Pro Leu Cys Met Ile Thr Asp Tyr Met Glu Asn
 435 440 445

Gly Asp Leu Asn Gln Phe Leu Ser Ala His Gln Leu Glu Asp Lys Ala
 450 455 460

Ala Glu Gly Ala Pro Gly Asp Gly Gln Ala Ala Gln Gly Pro Thr Ile
 465 470 475 480

Ser Tyr Pro Met Leu Leu His Val Ala Ala Gln Ile Ala Ser Gly Met
 485 490 495

Arg Tyr Leu Ala Thr Leu Asn Phe Val His Arg Asp Leu Ala Thr Arg
 500 505 510

Asn Cys Leu Val Gly Glu Asn Phe Thr Ile Lys Ile Ala Asp Phe Gly
 515 520 525

685

Met Ser Arg Asn Leu Tyr Ala Gly Asp Tyr Tyr Arg Val Gln Gly Arg
 530 535 540

Ala Val Leu Pro Ile Arg Trp Met Ala Trp Glu Cys Ile Leu Met Gly
 545 550 555 560

Lys Phe Thr Thr Ala Ser Asp Val Trp Ala Phe Gly Val Thr Leu Trp
 565 570 575

Glu Val Leu Met Leu Cys Arg Ala Gln Pro Phe Gly Gln Leu Thr Asp
 580 585 590

Glu Gln Val Ile Glu Asn Ala Gly Glu Phe Phe Arg Asp Gln Gly Arg
 595 600 605

Gln Val Tyr Leu Ser Arg Pro Pro Ala Cys Pro Gln Ala Tyr Met Ser
 610 615 620

<210> 739

<211> 477

<212> PRT

<213> Homo sapiens

<400> 739

Phe Gly Thr Ser Trp Cys Ser Met Met Leu Pro Pro Trp Thr Leu Gly
 1 5 10 15

Leu Leu Leu Leu Ala Thr Val Arg Gly Lys Glu Val Cys Tyr Gly Gln
 20 25 30

Leu Gly Cys Phe Ser Asp Glu Lys Pro Trp Ala Gly Thr Leu Gln Arg
 35 40 45

Pro Val Lys Leu Leu Pro Trp Ser Pro Glu Asp Ile Asp Thr Arg Phe
 50 55 60

Leu Leu Tyr Thr Asn Glu Asn Pro Asn Asn Phe Gln Leu Ile Thr Gly
 65 70 75 80

Thr Glu Pro Asp Thr Ile Glu Ala Ser Asn Phe Gln Leu Asp Arg Lys
 85 90 95

Thr Arg Phe Ile Ile His Gly Phe Leu Asp Lys Ala Glu Asp Ser Trp
 100 105 110

Pro Ser Asp Met Cys Lys Lys Met Phe Glu Val Glu Lys Val Asn Cys

686

115	120	125
Ile Cys Val Asp Trp Arg His Gly Ser Arg Ala Met Tyr Thr Gln Ala		
130	135	140
Val Gln Asn Ile Arg Val Val Gly Ala Glu Thr Ala Phe Leu Ile Gln		
145	150	155
Ala Leu Ser Thr Gln Leu Gly Tyr Ser Leu Glu Asp Val His Val Ile		
165	170	175
Gly His Ser Leu Gly Ala His Thr Ala Ala Glu Ala Gly Arg Arg Leu		
180	185	190
Gly Gly Arg Val Gly Arg Ile Thr Gly Leu Asp Pro Ala Gly Pro Cys		
195	200	205
Phe Gln Asp Glu Pro Glu Glu Val Arg Leu Asp Pro Ser Asp Ala Val		
210	215	220
Phe Val Asp Val Ile His Thr Asp Ser Ser Pro Ile Val Pro Ser Leu		
225	230	235
Gly Phe Gly Met Ser Gln Lys Val Gly His Leu Asp Phe Phe Pro Asn		
245	250	255
Gly Gly Lys Glu Met Pro Gly Cys Lys Lys Asn Val Leu Ser Thr Ile		
260	265	270
Thr Asp Ile Asp Gly Ile Trp Glu Gly Ile Gly Gly Phe Val Ser Cys		
275	280	285
Asn His Leu Arg Ser Phe Glu Tyr Tyr Ser Ser Ser Val Leu Asn Pro		
290	295	300
Asp Gly Phe Leu Gly Tyr Pro Cys Ala Ser Tyr Asp Glu Phe Gln Glu		
305	310	315
Ser Lys Cys Phe Pro Cys Pro Ala Glu Gly Cys Pro Lys Met Gly His		
325	330	335
Tyr Ala Asp Gln Phe Lys Gly Lys Thr Ser Ala Val Glu Gln Thr Phe		
340	345	350
Phe Leu Asn Thr Gly Glu Ser Gly Asn Phe Thr Ser Trp Arg Tyr Lys		
355	360	365
Val Ser Val Thr Leu Ser Gly Lys Glu Lys Val Asn Gly Tyr Ile Arg		
370	375	380
Ile Ala Leu Tyr Gly Ser Asn Glu Asn Ser Lys Gln Tyr Glu Ile Phe		

687

385 390 395 400
 Lys Gly Ser Leu Lys Pro Asp Ala Ser His Thr Cys Ala Ile Asp Val
 405 410 415
 Asp Phe Asn Val Gly Lys Ile Gln Lys Val Lys Phe Leu Trp Asn Lys
 420 425 430
 Arg Gly Ile Asn Leu Ser Glu Pro Lys Leu Gly Ala Ser Gln Ile Thr
 435 440 445
 Val Gln Ser Gly Glu Asp Gly Thr Glu Tyr Asn Phe Cys Ser Ser Asp
 450 455 460
 Thr Val Glu Glu Asn Val Leu Gln Ser Leu Tyr Pro Cys
 465 470 475

<210> 740
 <211> 303
 <212> PRT
 <213> Homo sapiens

<400> 740
 Asp Phe Arg Thr Ala Pro Gly Arg Arg Gly Arg Arg Arg Arg Thr Glu
 1 5 10 15
 Arg Pro Gly Arg Gly Gly Pro Ala Leu Gly Ser Gln Asp Ser Arg Gly
 20 25 30
 Ser Arg Val Arg Arg Ala Ala Ala Gly Leu Ser His Cys Ser Pro Pro
 35 40 45
 Ala Arg Leu Pro Ser Gly Ala Met Ala Gly Ser Ser Ser Leu Glu Ala
 50 55 60
 Val Arg Arg Lys Ile Arg Ser Leu Gln Glu Gln Ala Asp Ala Ala Glu
 65 70 75 80
 Glu Arg Ala Gly Thr Leu Gln Arg Glu Leu Asp His Glu Arg Lys Leu
 85 90 95
 Arg Glu Thr Ala Glu Ala Asp Val Ala Ser Leu Asn Arg Arg Ile Gln
 100 105 110
 Leu Val Glu Glu Glu Leu Asp Arg Ala Gln Glu Arg Leu Ala Thr Ala
 115 120 125
 Leu Gln Lys Leu Glu Glu Ala Glu Lys Ala Ala Asp Glu Ser Glu Arg
 130 135 140

688

Gly Met Lys Val Ile Glu Ser Arg Ala Gln Lys Asp Glu Glu Lys Met
145 150 155 160

Glu Ile Gln Glu Ile Gln Leu Lys Glu Ala Lys His Ile Ala Glu Asp
165 170 175

Ala Asp Arg Lys Tyr Glu Glu Val Ala Arg Lys Leu Val Ile Ile Glu
180 185 190

Ser Asp Leu Glu Arg Ala Glu Glu Arg Ala Glu Leu Ser Glu Gly Gln
195 200 205

Val Arg Gln Leu Glu Glu Gln Leu Arg Ile Met Asp Gln Thr Leu Lys
210 215 220

Ala Leu Met Ala Ala Glu Asp Lys Tyr Ser Gln Lys Glu Asp Arg Tyr
225 230 235 240

Glu Glu Glu Ile Lys Val Leu Ser Asp Lys Leu Lys Glu Ala Glu Thr
245 250 255

Arg Ala Glu Phe Ala Glu Arg Ser Val Thr Lys Leu Glu Lys Ser Ile
260 265 270

Asp Asp Leu Glu Glu Lys Val Ala His Ala Lys Glu Glu Asn Leu Ser
275 280 285

Met His Gln Met Leu Asp Gln Thr Leu Leu Glu Leu Asn Asn Met
290 295 300

<210> 741

<211> 363

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (2)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (144)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (340)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (344)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 741

His	Xaa	Pro	Arg	Leu	Pro	Ala	Leu	Pro	Pro	Arg	Leu	Leu	Ser	Pro	Ser
1				5					10					15	
Ala	Ala	Thr	Met	Ser	Ala	Ser	Ala	Val	Phe	Ile	Leu	Asp	Val	Lys	Gly
			20					25					30		
Lys	Pro	Leu	Ile	Ser	Arg	Asn	Tyr	Lys	Gly	Asp	Val	Ala	Met	Ser	Lys
		35					40					45			
Ile	Glu	His	Phe	Met	Pro	Leu	Leu	Val	Gln	Arg	Glu	Glu	Glu	Gly	Ala
	50					55					60				
Leu	Ala	Pro	Leu	Leu	Ser	His	Gly	Gln	Val	His	Phe	Leu	Trp	Ile	Lys
65					70					75					80
His	Ser	Asn	Leu	Tyr	Leu	Val	Ala	Thr	Thr	Ser	Lys	Asn	Ala	Asn	Ala
			85						90					95	
Ser	Leu	Val	Tyr	Ser	Phe	Leu	Tyr	Lys	Thr	Ile	Glu	Val	Phe	Cys	Glu
		100						105					110		
Tyr	Phe	Lys	Glu	Leu	Glu	Glu	Glu	Ser	Ile	Arg	Asp	Asn	Phe	Val	Ile
		115					120					125			
Val	Tyr	Glu	Leu	Leu	Asp	Glu	Leu	Met	Asp	Phe	Gly	Phe	Pro	Gln	Xaa
	130					135					140				
Thr	Asp	Ser	Lys	Ile	Leu	Gln	Glu	Tyr	Ile	Thr	Gln	Gln	Ser	Asn	Lys
145					150					155					160
Leu	Glu	Thr	Gly	Lys	Ser	Arg	Val	Pro	Pro	Thr	Val	Thr	Asn	Ala	Val
			165						170					175	
Ser	Trp	Arg	Ser	Glu	Gly	Ile	Lys	Tyr	Lys	Lys	Asn	Glu	Val	Phe	Ile
		180					185						190		
Asp	Val	Ile	Glu	Ser	Val	Asn	Leu	Leu	Val	Asn	Ala	Asn	Gly	Ser	Val
	195						200					205			
Leu	Leu	Ser	Glu	Ile	Val	Gly	Thr	Ile	Lys	Leu	Lys	Val	Phe	Leu	Ser
	210					215					220				
Gly	Met	Pro	Glu	Leu	Arg	Leu	Gly	Leu	Asn	Asp	Arg	Val	Leu	Phe	Glu

690

225 230 235 240
 Leu Thr Gly Arg Ser Lys Asn Lys Ser Val Glu Leu Glu Asp Val Lys
 245 250 255
 Phe His Gln Cys Val Arg Leu Ser Arg Phe Asp Asn Asp Arg Thr Ile
 260 265 270
 Ser Phe Ile Pro Pro Asp Gly Asp Phe Glu Leu Met Ser Tyr Arg Leu
 275 280 285
 Ser Thr Gln Val Lys Pro Leu Ile Trp Ile Glu Ser Val Ile Glu Lys
 290 295 300
 Phe Ser His Ser Arg Val Glu Ile Met Val Lys Ala Lys Gly Gln Phe
 305 310 315 320
 Lys Lys Gln Ser Val Ala Asn Gly Val Glu Ile Ser Val Pro Val Pro
 325 330 335
 Ser Asp Ala Xaa Ser Pro Arg Xaa Lys Thr Ser Val Gly Ser Ala Lys
 340 345 350
 Leu Cys Ala Gly Glu Lys Arg Arg Asp Leu Glu
 355 360

<210> 742

<211> 65

<212> PRT

<213> Homo sapiens

<400> 742

Met Met Glu Gly Ile Ile Leu Gly Tyr Leu Ala Leu Phe Phe Ser Lys
 1 5 10 15
 Lys Lys Ala Leu Leu Thr Thr Thr Phe Met Glu Ile Cys Arg Gly Lys
 20 25 30
 Tyr Phe Ile Gly His Lys Lys His His Asn Ile Thr Asn Leu Ile Phe
 35 40 45
 Phe Lys Cys Glu Leu Asn Pro Asn Ser His Leu Tyr Lys Met Thr Ile
 50 55 60
 Gly
 65

691

<210> 743
 <211> 95
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (4)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 743
 Thr Glu Lys Xaa Ile Lys Ile Ser Gly Phe Phe Leu Gly Tyr His Tyr
 1 5 10 15
 Cys Leu Ile Ser Leu Cys Gln Val Tyr Arg Thr Cys His Thr Phe Met
 20 25 30
 Ile Ser Ser Thr Glu Lys Leu Leu Ile Gln Ile Ser Pro Gly His Val
 35 40 45
 Arg Gln Asn Ile Ala Gly Trp Asp Phe Lys Val Ser Asp Asp Ala Phe
 50 55 60
 Pro Pro Ser Thr Asp Pro Pro Ala Pro Leu Ala Gly His Gly Glu Ala
 65 70 75 80
 Glu Ser His Leu Thr Ile Gln Lys Tyr Met Thr Thr Ser Pro Leu
 85 90 95

<210> 744
 <211> 237
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (207)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 744
 Arg Gly Gly Arg Ala Arg Gly Gly Gln Gly Pro Arg Leu Asn Ile Cys
 1 5 10 15
 Gly Ile Cys Gly Lys Ser Phe Gly Arg Gly Ser Thr Leu Ile Gln His
 20 25 30
 Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Glu Val Cys Ser
 35 40 45

692

Lys Ala Phe Ser Gln Ser Ser Asp Leu Ile Lys His Gln Arg Thr His
 50 55 60
 Thr Gly Glu Arg Pro Tyr Lys Cys Pro Arg Cys Gly Lys Ala Phe Ala
 65 70 75 80
 Asp Ser Ser Tyr Leu Leu Arg His Gln Arg Thr His Ser Gly Gln Lys
 85 90 95
 Pro Tyr Lys Cys Pro His Cys Gly Lys Ala Phe Gly Asp Ser Ser Tyr
 100 105 110
 Leu Leu Arg His Gln Arg Thr His Ser His Glu Arg Pro Tyr Ser Cys
 115 120 125
 Thr Glu Cys Gly Lys Cys Tyr Ser Gln Asn Ser Ser Leu Arg Ser Ile
 130 135 140
 Arg Gly Cys Thr Pro Val Arg Gly Pro Ser Ala Val Ala Ser Ala Ala
 145 150 155 160
 Arg Ala Ser Pro Ser Gly Arg Pro Leu Ser Pro Met Pro Ala Ala Thr
 165 170 175
 Pro Gly Arg Ser Pro Ser Ser Ala Leu Ser Ala Ala Ser Ala Leu Ala
 180 185 190
 Arg Ala Arg Cys Trp Pro Ser Thr Pro Ala Pro Thr Cys Gln Xaa Ala
 195 200 205
 Pro Thr Ala Ala Pro Thr Ala Ala Arg Pro Ser Ile Ala Pro Pro Leu
 210 215 220
 Ser Ser Ser Thr Ser Ala Pro Thr Arg Ala Ser Gly Pro
 225 230 235

<210> 745

<211> 267

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (191)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 745

Asp Thr Ser Val Thr Met Trp Phe Leu Val Leu Cys Leu Ala Leu Ser
 1 5 10 15

Leu Gly Gly Thr Gly Ala Ala Pro Pro Ile Gln Ser Arg Ile Val Gly
 20 25 30
 Gly Trp Glu Cys Glu Gln His Ser Gln Pro Trp Gln Ala Ala Leu Tyr
 35 40 45
 His Phe Ser Thr Phe Gln Cys Gly Gly Ile Leu Val His Arg Gln Trp
 50 55 60
 Val Leu Thr Ala Ala His Cys Ile Ser Asp Asn Tyr Gln Leu Trp Leu
 65 70 75 80
 Gly Arg His Asn Leu Phe Asp Asp Glu Asn Thr Ala Gln Phe Val His
 85 90 95
 Val Ser Glu Ser Phe Pro His Pro Gly Phe Asn Met Ser Leu Leu Glu
 100 105 110
 Asn His Thr Arg Gln Ala Asp Glu Asp Tyr Ser His Asp Leu Met Leu
 115 120 125
 Leu Arg Leu Thr Glu Pro Ala Asp Thr Ile Thr Asp Ala Val Lys Val
 130 135 140
 Val Glu Leu Pro Thr Gln Glu Pro Glu Val Gly Ser Thr Cys Leu Ala
 145 150 155 160
 Ser Gly Trp Gly Ser Ile Glu Pro Glu Asn Phe Ser Phe Pro Asp Asp
 165 170 175
 Leu Gln Cys Val Asp Leu Lys Ile Leu Pro Asn Asp Glu Cys Xaa Lys
 180 185 190
 Ala His Val Gln Lys Val Thr Asp Phe Met Leu Cys Val Gly His Leu
 195 200 205
 Glu Gly Gly Lys Asp Thr Cys Val Gly Asp Ser Gly Gly Pro Leu Met
 210 215 220
 Cys Asp Gly Val Leu Gln Gly Val Thr Ser Trp Gly Tyr Val Pro Cys
 225 230 235 240
 Gly Thr Pro Asn Lys Pro Ser Val Ala Val Arg Val Leu Ser Tyr Val
 245 250 255
 Lys Trp Ile Glu Asp Thr Ile Ala Glu Asn Ser
 260 265

694

<210> 746
<211> 169
<212> PRT
<213> Homo sapiens

<400> 746
Arg Leu Arg Ser Gly Pro Trp Ile Ser Ser Lys Met Ala Ala Arg Ser
1 5 10 15
Val Ser Gly Ile Thr Arg Arg Val Phe Met Trp Thr Val Ser Gly Thr
20 25 30
Pro Cys Arg Glu Phe Trp Ser Arg Phe Arg Lys Glu Lys Glu Pro Val
35 40 45
Val Val Glu Thr Val Glu Glu Lys Lys Glu Pro Ile Leu Val Cys Pro
50 55 60
Pro Leu Arg Ser Arg Ala Tyr Thr Pro Pro Glu Asp Leu Gln Ser Arg
65 70 75 80
Leu Glu Ser Tyr Val Lys Glu Val Phe Gly Ser Ser Leu Pro Ser Asn
85 90 95
Trp Gln Asp Ile Ser Leu Glu Asp Ser Arg Leu Lys Phe Asn Leu Leu
100 105 110
Ala His Leu Ala Asp Asp Leu Gly His Val Val Pro Asn Ser Arg Leu
115 120 125
His Gln Met Cys Arg Val Arg Asp Val Leu Asp Phe Tyr Asn Val Pro
130 135 140
Ile Gln Asp Arg Ser Lys Phe Asp Glu Leu Ser Ala Ser Asn Leu Pro
145 150 155 160
Pro Asn Leu Lys Ile Thr Trp Ser Tyr
165

<210> 747
<211> 414
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (14)
<223> Xaa equals any of the naturally occurring L-amino acids

695

<400> 747

Cys Leu Val Asn Leu Pro Pro Thr Gln Thr Gln Ala Val Xaa Arg Pro
 1 5 10 15
 Ser Thr Leu Leu Pro Asn Tyr Val Leu Lys Pro Phe Phe Pro Asn Leu
 20 25 30
 Phe Pro Pro Pro Glu Ser Trp Phe Gly Ser Trp Leu Pro Ile Cys Leu
 35 40 45
 Leu Leu Leu Thr Trp Val Asn Cys Ser Ser Val Arg Trp Ala Thr Arg
 50 55 60
 Val Gln Asp Ile Phe Thr Ala Gly Lys Leu Leu Ala Leu Ala Leu Ile
 65 70 75 80
 Ile Ile Met Gly Ile Val Gln Ile Cys Lys Gly Glu Tyr Phe Trp Leu
 85 90 95
 Glu Pro Lys Asn Ala Phe Glu Asn Phe Gln Glu Pro Asp Ile Gly Leu
 100 105 110
 Val Ala Leu Ala Phe Leu Gln Gly Ser Phe Ala Tyr Gly Gly Trp Asn
 115 120 125
 Phe Leu Asn Tyr Val Thr Glu Glu Leu Val Asp Pro Tyr Lys Asn Leu
 130 135 140
 Pro Arg Ala Ile Phe Ile Ser Ile Pro Leu Val Thr Phe Val Tyr Val
 145 150 155 160
 Phe Ala Asn Val Ala Tyr Val Thr Ala Met Ser Pro Gln Glu Leu Leu
 165 170 175
 Ala Ser Asn Ala Val Ala Val Thr Phe Gly Glu Lys Leu Leu Gly Val
 180 185 190
 Met Ala Trp Ile Met Pro Ile Ser Val Ala Leu Ser Thr Phe Gly Gly
 195 200 205
 Val Asn Gly Ser Leu Phe Thr Ser Ser Arg Leu Phe Phe Ala Gly Ala
 210 215 220
 Arg Glu Gly His Leu Pro Ser Val Leu Ala Met Ile His Val Lys Arg
 225 230 235 240
 Cys Thr Pro Ile Pro Ala Leu Leu Phe Thr Cys Ile Ser Thr Leu Leu
 245 250 255
 Met Leu Val Thr Ser Asp Met Tyr Thr Leu Ile Asn Tyr Val Gly Phe
 260 265 270

Ile Asn Tyr Leu Phe Tyr Gly Val Thr Val Ala Gly Gln Ile Val Leu
275 280 285

Arg Trp Lys Lys Pro Asp Ile Pro Arg Pro Ile Lys Ile Asn Leu Leu
290 295 300

Phe Pro Ile Ile Tyr Leu Leu Phe Trp Ala Phe Leu Leu Val Phe Ser
305 310 315 320

Leu Trp Ser Glu Pro Val Val Cys Gly Ile Gly Leu Ala Ile Met Leu
325 330 335

Thr Gly Val Pro Val Tyr Phe Leu Gly Val Tyr Trp Gln His Lys Pro
340 345 350

Lys Cys Phe Ser Asp Phe Ile Glu Leu Leu Thr Leu Val Ser Gln Lys
355 360 365

Met Cys Val Val Val Tyr Pro Glu Val Glu Arg Gly Ser Gly Thr Glu
370 375 380

Glu Ala Asn Glu Asp Met Glu Glu Gln Gln Gln Pro Met Tyr Gln Pro
385 390 395 400

Thr Pro Thr Lys Asp Lys Asp Val Ala Gly Gln Pro Gln Pro
405 410

<210> 748

<211> 78

<212> PRT

<213> Homo sapiens

<400> 748

His Leu Ser Gln Glu His Leu Ser Lys Ser Ile Tyr Pro Lys Ser Ile
1 5 10 15

Tyr Pro Asp Asp Phe Ser Ile Tyr Pro Lys Ser Ile Tyr Pro Lys Asp
20 25 30

Ser Ile Tyr Pro Lys Ser Ile Tyr Pro Arg Ala Phe Phe Pro Arg Leu
35 40 45

Phe Ile Pro Lys Ile Leu Ala Phe Ile Pro Arg Ala Phe Thr Gln Glu
50 55 60

His Leu Ser Gln Gly Ile Leu Phe Cys Phe Val Leu Phe Phe
65 70 75

<210> 749
<211> 93
<212> PRT
<213> Homo sapiens

<400> 749

Met Cys Gly Cys Ser Arg His Phe Ser Val Val Val Cys Ser His Phe
1 5 10 15
Gly Pro Thr Pro Ala Ser Leu Ala Thr Leu Gln Leu Cys Ser Asp Phe
20 25 30
Cys Val Tyr Ala Trp Cys Ala Ser Leu Ala Ala Phe Ser Ser Met Gln
35 40 45
Pro Gly Val Asp Val Gly Lys Arg Asp Ala Phe Leu Leu Trp Lys Leu
50 55 60
Ser Gly Lys Leu Val Ser Ile Ser Pro Pro Leu Pro Gly Leu Pro Cys
65 70 75 80
Thr Pro Lys Asp Phe Val Gln Met Gly Ser Ser Ile Phe
85 90

<210> 750
<211> 91
<212> PRT
<213> Homo sapiens

<220>

<221> SITE

<222> (31)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 750

Leu Cys Phe Trp His Ile Thr Val Leu Cys His Tyr Tyr Lys Val Lys
1 5 10 15
His Leu Gln Arg Arg Met Ser Leu Lys Met Arg Asp Leu Leu Xaa Ile
20 25 30
Asn Met Pro Met Arg Ala Tyr Leu Ile Ser Leu Tyr Asn Met Gln Pro
35 40 45
Asn Gln Thr Phe Thr Pro Ala Glu Lys Cys Cys Pro Gly Glu Lys Glu
50 55 60

698

Ile Tyr Lys Asp Arg Leu Ser Pro Phe Phe Cys Cys Ser Thr Lys His
65 70 75 80

Ser Lys Lys Leu Glu Ser Phe Thr Leu Glu Ile
85 90

<210> 751

<211> 94

<212> PRT

<213> Homo sapiens

<400> 751

Val Arg Cys Ser Phe Gln Leu Thr Ser Gly Arg Arg Thr Ser Ala Met
1 5 10 15

Lys Val Thr Gly Ile Phe Leu Leu Ser Ala Leu Ala Leu Leu Ser Leu
20 25 30

Ser Gly Asn Thr Gly Ala Asp Ser Leu Gly Arg Glu Ala Lys Cys Tyr
35 40 45

Asn Glu Leu Asn Gly Cys Thr Lys Ile Tyr Asp Pro Val Cys Gly Thr
50 55 60

Asp Gly Asn Thr Tyr Pro Asn Glu Cys Val Leu Cys Phe Glu Asn Arg
65 70 75 80

Lys Arg Gln Thr Ser Ile Leu Ile Gln Lys Ser Gly Pro Cys
85 90

<210> 752

<211> 78

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 752

Val Arg Gly Ala Gly Val Leu Glu Pro Gln Thr Ala Gln Glu Ala Pro
1 5 10 15

Gly Arg Cys Arg Gly Ala Leu Trp Trp Val Pro Pro Thr Lys Arg Glu
20 25 30

699

Gly Leu Val Cys Pro Ser Pro Ser Gly Thr Thr Gln Pro Ser Ala Ala
 35 40 45

Leu Ser Gln Thr Phe Leu Pro Cys Pro Ala Glu Leu Val Tyr Gln Glu
 50 55 60

Val Ile Leu Gln Pro Glu Arg Xaa Val Leu Trp Lys Arg Gln
 65 70 75

<210> 753

<211> 174

<212> PRT

<213> Homo sapiens

<400> 753

Ala Arg Asp Ser Leu Pro Leu Ser Met Ala Gln Thr Asn Ser Phe Phe
 1 5 10 15

Met Leu Ile Ser Ser Leu Met Phe Leu Ser Leu Ser Gln Gly Gln Glu
 20 25 30

Ser Gln Thr Glu Leu Pro Asn Pro Arg Ile Ser Cys Pro Glu Gly Thr
 35 40 45

Asn Ala Tyr Arg Ser Tyr Cys Tyr Tyr Phe Asn Glu Asp Pro Glu Thr
 50 55 60

Trp Val Asp Ala Asp Leu Tyr Cys Gln Asn Met Asn Ser Gly Asn Leu
 65 70 75 80

Val Ser Val Leu Thr Gln Ala Glu Gly Ala Phe Val Ala Ser Leu Ile
 85 90 95

Lys Glu Ser Ser Thr Asp Asp Ser Asn Val Trp Ile Gly Leu His Asp
 100 105 110

Pro Lys Lys Asn Arg Arg Trp His Trp Ser Ser Gly Ser Leu Val Ser
 115 120 125

Tyr Lys Ser Trp Asp Thr Gly Ser Pro Ser Ser Ala Asn Ala Gly Tyr
 130 135 140

Cys Ala Ser Leu Thr Ser Cys Ser Gly Phe Lys Lys Trp Lys Asp Glu
 145 150 155 160

Ser Cys Glu Lys Lys Phe Ser Phe Val Cys Lys Phe Lys Asn
 165 170

700

<210> 754

<211> 85

<212> PRT

<213> Homo sapiens

<400> 754

Cys Arg Pro Arg Ser Gly Ile Pro Gly Glu Glu Glu Glu Glu Glu Glu
1 5 10 15

Asp Ser Gln Ala Glu Val Leu Lys Val Ile Arg Gln Ser Ala Gly Gln
20 25 30

Lys Thr Thr Cys Gly Gln Gly Leu Glu Gly Pro Trp Glu Arg Pro Pro
35 40 45

Pro Leu Asp Glu Ser Glu Arg Asp Gly Gly Ser Glu Asp Gln Val Glu
50 55 60

Asp Pro Ala Leu Ser Glu Pro Gly Glu Glu Pro Gln Arg Pro Ser Pro
65 70 75 80

Ser Glu Pro Gly Thr
85

<210> 755

<211> 121

<212> PRT

<213> Homo sapiens

<400> 755

Gly Arg Val Gly Glu Gln Thr Val Pro Tyr Gly Leu Ser Asn Tyr Arg
1 5 10 15

Gly Ser Phe Arg Gly Lys Arg Ser Ala Gly Pro Leu Pro Gly Asn Leu
20 25 30

Gln Leu Ser His Arg Pro His Leu Arg Cys Ala Cys Val Gly Arg Tyr
35 40 45

Asp Lys Ala Cys Leu His Phe Cys Thr Gln Thr Leu Asp Val Ser Ser
50 55 60

Asn Ser Arg Thr Ala Glu Lys Thr Asp Lys Glu Glu Glu Gly Lys Val
65 70 75 80

Glu Val Lys Asp Gln Gln Ser Lys Gln Ala Leu Asp Leu His His Pro
85 90 95

Lys Leu Met Pro Gly Ser Gly Leu Ala Leu Ala Pro Ser Thr Cys Pro
100 105 110

Arg Cys Leu Phe Gln Glu Gly Ala Pro
115 120

<210> 756
<211> 39
<212> PRT
<213> Homo sapiens

<400> 756
Gly Phe Ser Cys Leu Ser Leu Leu Ser Ser Cys Asp Tyr Arg His Ala
1 5 10 15

Pro Pro Cys Leu Ala Asn Phe Ile Phe Phe Ser Arg Asp Arg Ile Ser
20 25 30

Pro Cys Trp Ser Gly Trp Ser
35

<210> 757
<211> 63
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (56)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 757
Thr Ser Ser Thr Ile Asn Cys Ser Leu Gly Thr Phe Tyr Ala Gln Asn
1 5 10 15

Cys Ala Pro Ser Ser Glu Gln Gln Val Phe Asn Gly Pro Cys Asp Glu
20 25 30

Lys Gly Pro Ile Lys Ala Ala Gly Met Gly His Ser Pro Thr Pro His
35 40 45

Gly Pro Gly His Cys His Ser Xaa Cys Pro Ala Ser Pro Gly Leu
50 55 60

<210> 758

<211> 65

<212> PRT

<213> Homo sapiens

<400> 758

Leu Leu Asp Cys Phe Cys Asp Thr Asp Thr Ser Pro Leu Ser Glu His
1 5 10 15

Pro Leu Pro Leu Asp Ser Val His Arg Lys Leu Val Ala Pro Leu Asn
20 25 30

Thr Leu Phe Leu Pro Cys Asn Thr Ala Ser Asp Phe Glu Pro Lys Asn
35 40 45

Lys Asp Tyr Ser Ser Gln Thr Pro Ser Gln Ile Asn Phe Val Thr Lys
50 55 60

Leu

65

<210> 759

<211> 101

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (20)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (49)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 759

His Pro Ala Ser Asn Leu Gly Asp Phe Arg Arg Cys Leu Asn Pro Asp
1 5 10 15

Leu Ser Val Xaa Trp Pro His Cys Glu Pro Arg Asn Ala Thr Pro Trp
20 25 30

Lys Pro His Thr Leu Leu Ser Pro Ser Val Leu Ile Pro Val Leu Leu
35 40 45

Xaa Val Ser Pro Ser Trp Leu Phe Leu Glu Ser Leu Ser Phe Pro His
50 55 60

Phe Pro Leu Pro Ala Ala Val Leu Ser Pro Val Ala Leu Asp Leu His

703

65 70 75 80
Ser Trp Ser Asn Thr Leu Asn Ser Asn Thr Ser Val Phe Leu Pro His
 85 90 95
Pro Leu Asp Lys Ser
 100

<210> 760
<211> 61
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (61)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 760
Ile Arg Ile Ala Ala Leu Asp Asp Phe Arg Thr Ser Leu Thr Met Ser
1 5 10 15
Ser Thr Arg Ser Gln Asn Pro His Gly Leu Lys Gln Ile Gly Leu Asp
 20 25 30
Gln Ile Xaa Gly Arg Pro Gln Ser Xaa Ala Ser Ser Arg Cys Tyr Thr
 35 40 45
Arg Ala Glu His Gly Pro Ser Ser Arg Tyr Met Glu Xaa
50 55 60

<210> 761
<211> 255
<212> PRT
<213> H mo sapiens

<220>

<221> SITE

<222> (186)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (195)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (209)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 761

Leu Thr Pro Ser Gly Phe Arg Ser Gly Arg Ser Val Pro Thr Met Gly
 1 5 10 15

Leu Glu Leu Tyr Leu Asp Leu Leu Ser Gln Pro Cys Arg Ala Val Tyr
 20 25 30

Ile Phe Ala Lys Lys Asn Asp Ile Pro Phe Glu Leu Arg Ile Val Asp
 35 40 45

Leu Ile Lys Gly Gln His Leu Ser Asp Ala Phe Ala Gln Val Asn Pro
 50 55 60

Leu Lys Lys Val Pro Ala Leu Lys Asp Gly Asp Phe Thr Leu Thr Glu
 65 70 75 80

Ser Val Ala Ile Leu Leu Tyr Leu Thr Arg Lys Tyr Lys Val Pro Asp
 85 90 95

Tyr Trp Tyr Pro Gln Asp Leu Gln Ala Arg Ala Arg Val Asp Glu Tyr
 100 105 110

Leu Ala Trp Gln His Thr Thr Leu Arg Arg Ser Cys Leu Arg Ala Leu
 115 120 125

Trp His Lys Val Met Phe Pro Val Phe Leu Gly Glu Pro Val Ser Pro
 130 135 140

Gln Thr Leu Ala Ala Thr Leu Ala Glu Leu Asp Val Thr Leu Gln Leu
 145 150 155 160

Leu Glu Asp Lys Phe Leu Gln Asn Lys Ala Phe Leu Thr Gly Pro His
 165 170 175

Ile Ser Leu Ala Asp Leu Val Ala Ile Xaa Glu Leu Met His Pro Val
 180 185 190

705

Gly Ala Xaa Leu Pro Ser Leu Arg Arg Pro Thr Gln Ala Gly His Met
 195 200 205

Xaa Ala Gly Val Glu Ala Ala Val Gly Glu Asp Leu Phe Gln Glu Ala
 210 215 220

His Glu Val Ile Leu Lys Ala Lys Asp Asp Phe Pro Pro Ala Asp Pro
 225 230 235 240

Thr Ile Lys Gln Lys Leu Met Pro Trp Val Leu Ala Met Ile Arg
 245 250 255

<210> 762

<211> 85

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 762

Asp Glu Tyr Leu Ala Trp Gln His Thr Thr Leu Arg Arg Ser Cys Leu
 1 5 10 15

Arg Ala Leu Trp His Pro Val Gly Ala Gly Cys Gln Val Phe Glu Gly
 20 25 30

Arg Pro Lys Leu Ala Thr Trp Arg Xaa Arg Val Glu Ala Ala Val Gly
 35 40 45

Glu Asp Leu Phe Gln Glu Ala His Glu Val Ile Leu Lys Ala Lys Asp
 50 55 60

Phe Pro Pro Ala Asp Pro Thr Ile Lys Gln Lys Leu Met Pro Trp Val
 65 70 75 80

Leu Ala Met Ile Arg
 85

<210> 763

<211> 136

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 763

His Glu Xaa Arg Glu His Ala Gly Pro Lys Met Ala Ala Ser Arg Tyr
 1 5 10 15

Arg Arg Phe Leu Lys Leu Cys Glu Glu Trp Pro Val Asp Glu Thr Lys
 20 25 30

Arg Gly Arg Asp Leu Gly Ala Tyr Leu Arg Gln Arg Val Ala Gln Ala
 35 40 45

Phe Arg Glu Gly Glu Asn Thr Gln Val Ala Glu Pro Glu Ala Cys Asp
 50 55 60

Gln Met Tyr Glu Ser Leu Ala Arg Leu His Ser Asn Tyr Tyr Lys His
 65 70 75 80

Lys Tyr Pro Arg Pro Arg Asp Thr Ser Phe Ser Gly Leu Ser Leu Glu
 85 90 95

Glu Tyr Lys Leu Ile Leu Ser Thr Asp Thr Leu Glu Glu Leu Lys Glu
 100 105 110

Ile Asp Lys Gly Met Trp Lys Lys Leu Gln Glu Lys Phe Ala Pro Lys
 115 120 125

Gly Pro Glu Glu Asp His Lys Ala
 130 135

<210> 764

<211> 302

<212> PRT

<213> Homo sapiens

<400> 764

Pro Gly Leu His Pro Gly Asn Arg Gly Leu Arg Ile Leu Leu Thr Leu
 1 5 10 15

Pro Pro Asn Trp Pro Gln Tyr Ile His Ser Leu Arg Lys Lys Asn Lys
 20 25 30

Val Pro Thr Ala Lys Lys Arg Asn Arg Ile Lys Arg Tyr Val Ala Ala
 35 40 45

Gly Arg Ala Ser Met Asn Ser Met Thr Ser Ala Val Pro Val Ala Asn
 50 55 60

Ser Val Leu Val Val Ala Pro His Asn Gly Tyr Pro Val Thr Pro Gly
 65 70 75 80
 Ile Met Ser His Val Pro Leu Tyr Pro Asn Ser Gln Pro Gln Val His
 85 90 95
 Leu Val Pro Gly Asn Pro Pro Ser Leu Val Ser Asn Val Asn Gly Gln
 100 105 110
 Pro Val Gln Lys Ala Leu Lys Glu Gly Lys Thr Leu Gly Ala Ile Gln
 115 120 125
 Ile Ile Ile Gly Leu Ala His Ile Gly Leu Gly Ser Ile Met Ala Thr
 130 135 140
 Val Leu Val Gly Glu Tyr Leu Ser Ile Ser Phe Tyr Gly Gly Phe Pro
 145 150 155 160
 Phe Trp Gly Gly Leu Trp Phe Ile Ile Ser Gly Ser Leu Ser Val Ala
 165 170 175
 Ala Glu Asn Gln Pro Tyr Ser Tyr Cys Leu Leu Ser Gly Ser Leu Gly
 180 185 190
 Leu Asn Ile Val Ser Ala Ile Cys Ser Ala Val Gly Val Ile Leu Phe
 195 200 205
 Ile Thr Asp Leu Ser Ile Pro His Pro Tyr Ala Tyr Pro Asp Tyr Tyr
 210 215 220
 Pro Tyr Ala Trp Gly Val Asn Pro Gly Met Ala Ile Ser Gly Val Leu
 225 230 235 240
 Leu Val Phe Cys Leu Leu Glu Phe Gly Ile Ala Cys Ala Ser Ser His
 245 250 255
 Phe Gly Cys Gln Leu Val Cys Cys Gln Ser Ser Asn Val Ser Val Ile
 260 265 270
 Tyr Pro Asn Ile Tyr Ala Ala Asn Pro Val Ile Thr Pro Glu Pro Val
 275 280 285
 Thr Ser Pro Pro Ser Tyr Ser Ser Glu Ile Gln Ala Asn Lys
 290 295 300

<210> 765

<211> 141

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (131)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (137)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 765

Lys Met Phe Arg Lys Gly Lys Lys Arg His Ser Ser Ser Ser Ser Gln
1 5 10 15

Ser Ser Glu Ile Ser Thr Lys Ser Lys Ser Val Asp Ser Ser Leu Gly
20 25 30

Gly Leu Ser Arg Ser Ser Thr Val Ala Ser Leu Asp Thr Asp Ser Thr
35 40 45

Lys Ser Ser Gly Gln Ser Asn Asn Asn Ser Asp Thr Cys Ala Glu Phe
50 55 60

Arg Ile Lys Tyr Val Gly Ala Ile Glu Lys Leu Lys Leu Ser Glu Gly
65 70 75 80

Lys Gly Leu Glu Gly Pro Leu Asp Leu Ile Asn Tyr Ile Asp Val Ala
85 90 95

Gln Gln Asp Gly Lys Leu Pro Phe Val Pro Pro Glu Glu Glu Phe Ile
100 105 110

Met Gly Val Ser Lys Tyr Gly Ile Lys Val Phe Asn Ile Arg Ser Ile
115 120 125

Cys Lys Xaa Tyr Asn Leu Leu Arg Xaa Leu Cys Phe Arg
130 135 140

<210> 766

<211> 55

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (21)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (22)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (23)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 766

Asn Leu Cys Asn Phe Leu Tyr Leu Leu Leu Phe His Gln Arg Asn Leu
 1 5 10 15

Lys Ser Phe Phe Xaa Xaa Xaa Lys Lys Lys Lys Lys Lys Lys Lys Lys
 20 25 30

Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
 35 40 45

Lys Lys Lys Gly Gly Arg Phe
 50 55

<210> 767

<211> 115

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (18)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 767

Thr Leu Asn Thr Tyr Leu Ser Phe Asn Val His Ile Asn Lys Ala Pro
 1 5 10 15

Ile Xaa Trp Ser Leu Glu Lys Lys Lys Ser Phe His Val Val Pro Arg
 20 25 30

Ser Arg Ser Arg Ser Ser Ser Gln Phe Glu Ser Arg Ser Arg Ser Ser
 35 40 45

Ser Arg Glu Arg Ser Arg Ser Arg Gly Ser Lys Ser Arg Ser Ser Ser
 50 55 60

Arg Ser Thr Gly Ala Leu Leu Pro His Glu Lys Asp Leu Ile Gln Val
 65 70 75 80

710

His His Leu Leu Leu Arg Gly Thr Glu Arg Glu Val Val Leu Asp Leu
 85 90 95

Leu His Leu Val Ile Ala Lys Lys Asp Glu Gln Asp His Gly His Pro
 100 105 110

Lys Ala Arg
 115

<210> 768
 <211> 303
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (257)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 768
 Val Asn Glu Ile Met Ile Leu Glu Gly Gly Gly Val Met Asn Leu Asn
 1 5 10 15

Pro Gly Asn Asn Leu Leu His Gln Pro Pro Ala Trp Thr Asp Ser Tyr
 20 25 30

Ser Thr Cys Asn Val Ser Ser Gly Phe Phe Gly Gly Gln Trp His Glu
 35 40 45

Ile His Pro Gln Tyr Trp Thr Lys Tyr Gln Val Trp Glu Trp Leu Gln
 50 55 60

His Leu Leu Asp Thr Asn Gln Leu Asp Ala Asn Cys Ile Pro Phe Gln
 65 70 75 80

Glu Phe Asp Ile Asn Gly Glu His Leu Cys Ser Met Ser Leu Gln Glu
 85 90 95

Phe Thr Arg Ala Ala Gly Thr Ala Gly Gln Leu Leu Tyr Ser Asn Leu
 100 105 110

Gln His Leu Lys Trp Asn Gly Gln Cys Ser Ser Asp Leu Phe Gln Ser
 115 120 125

Thr His Asn Val Ile Val Lys Thr Glu Gln Thr Glu Pro Ser Ile Met
 130 135 140

Asn Thr Trp Lys Asp Glu Asn Tyr Leu Tyr Asp Thr Asn Tyr Gly Ser

711

145		150		155		160
Thr Val Asp Leu Leu Asp Ser Lys Thr Phe Cys Arg Ala Gln Ile Ser						
	165		170		175	
Met Thr Thr Thr Ser His Leu Pro Val Glu Ser Pro Asp Met Lys Lys						
	180		185		190	
Glu Gln Asp Pro Pro Ala Lys Cys His Thr Lys Lys His Asn Pro Arg						
	195		200		205	
Gly Thr His Leu Trp Glu Phe Ile Arg Asp Ile Leu Leu Asn Pro Asp						
	210		215		220	
Lys Asn Pro Gly Leu Ile Lys Trp Glu Asp Arg Ser Glu Gly Val Phe						
	225		230		235	240
Arg Phe Leu Lys Ser Glu Ala Val Ala Gln Leu Trp Gly Lys Lys Lys						
	245		250		255	
Xaa Asn Ser Ser Met Thr Tyr Glu Lys Leu Ser Arg Ala Met Arg Tyr						
	260		265		270	
Tyr Tyr Lys Arg Glu Ile Leu Glu Arg Val Asp Gly Arg Arg Leu Val						
	275		280		285	
Tyr Lys Phe Gly Lys Asn Ala Arg Gly Trp Arg Glu Asn Glu Asn						
	290		295		300	

<210> 769

<211> 95

<212> PRT

<213> Homo sapiens

<400> 769

Asn Met Tyr Gly Thr Ser Cys Leu Ile Leu His Val Thr Ser Leu Leu											
1		5		10		15					
Tyr Ile Asp Glu Val Leu Val Thr Leu Ser Ser Asn Thr Leu Pro Leu											
	20		25		30						
Leu Phe Arg Glu Cys Leu Arg Asp Phe Leu Tyr Trp Phe Tyr Tyr Ser											
	35		40		45						
Asp Tyr Gly Leu Asp Leu Ser Ile Leu Leu Leu Pro Pro Gly Phe Leu											
	50		55		60						
Ile Ile His Pro Ser Lys Leu Ile Phe Cys Glu Ala Phe Val Ser Gln											
	65		70		75		80				

Ile Lys Thr Leu Leu Glu Pro Lys Val Val Ala Asp Gly Tyr Leu
 85 90 95

<210> 770

<211> 247

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (131)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 770

Gly Ser Arg Ser Arg Ala Ala Ala Arg Glu Gln Leu Pro Lys Ser Val
 1 5 10 15

Pro Cys Gly Ala Gly Ala Gly Arg Gly Phe Ala Glu Ala Pro Arg His
 20 25 30

Ser Glu Glu Val Arg Glu Arg Arg Gln Thr Thr Gly Asp Pro Gly Pro
 35 40 45

Ala Ala Arg Ala Glu Pro Ser Val Pro Ala Cys Val Pro Ala Cys Pro
 50 55 60

Arg Gly Cys Val Phe Ala Gly Val Cys Cys Val His Arg Cys Phe Cys
 65 70 75 80

Gly Arg Arg His Val Arg Thr Gly Trp Gly Cys Pro Ser Glu Pro Met
 85 90 95

Arg His Lys Ala Cys Arg Arg Leu Phe Gly Pro Val Asp Ser Glu Gln
 100 105 110

Leu Ser Arg Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln Glu Ala
 115 120 125

Arg Glu Xaa Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu Glu Gly
 130 135 140

Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys Leu Tyr
 145 150 155 160

Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly Gly Arg
 165 170 175

Arg Pro Gly Thr Ser Pro Ala Leu Leu Gln Gly Thr Ala Glu Glu Asp

713

180 185 190
His Val Asp Leu Ser Leu Ser Cys Thr Leu Val Pro Arg Ser Gly Glu
195 200 205
Gln Ala Glu Gly Ser Pro Gly Gly Pro Gly Asp Ser Gln Gly Arg Lys
210 215 220
Arg Arg Gln Thr Ser Met Thr Asp Phe Tyr His Ser Lys Arg Arg Leu
225 230 235 240
Ile Phe Ser Lys Arg Lys Pro
245

<210> 771
<211> 81
<212> PRT
<213> Homo sapiens

<400> 771
Cys Ile Cys Leu Ser Cys Ala Thr Gly Ala Ser Asn Gln His Ile His
1 5 10 15
Gln His Pro Ser Gly Gly Val His Gly Arg Val Pro Ser Leu Phe Leu
20 25 30
Leu His Phe Ser Phe Phe Ser Phe Leu Leu Lys Leu Leu Phe Asn Ser
35 40 45
Ala Lys Gly Ser Phe Phe Phe Ala Phe Leu Asn Leu Asn Phe Phe Asn
50 55 60
Leu His Phe Leu Val Leu Ile Phe Leu Tyr Ile Leu Leu Ala Met Ser
65 70 75 80
Phe

<210> 772
<211> 281
<212> PRT
<213> Homo sapiens

<400> 772
Ser Val Arg Ser Asn Ser Gly Ser Thr Thr Arg Pro Leu Ser Pro Pro
1 5 10 15

Ile Pro Arg Thr Ser Asn Lys Val Pro Val Val Gln Pro Ser His Ala
 20 25 30
 Val His Pro Leu Thr Pro Leu Ile Thr Tyr Ser Asp Glu His Phe Ser
 35 40 45
 Pro Gly Ser His Pro Ser His Ile Pro Ser Asp Val Asn Ser Lys Gln
 50 55 60
 Gly Met Ser Arg His Pro Pro Ala Pro Asp Ile Pro Thr Phe Tyr Pro
 65 70 75 80
 Leu Ser Pro Gly Gly Val Gly Gln Ile Thr Pro Pro Leu Gly Trp Gln
 85 90 95
 Gly Gln Pro Val Tyr Pro Ile Thr Gly Gly Phe Arg Gln Pro Tyr Pro
 100 105 110
 Ser Ser Leu Ser Val Asp Thr Ser Met Ser Arg Phe Ser His His Met
 115 120 125
 Ile Pro Gly Pro Pro Gly Pro His Thr Thr Gly Ile Pro His Pro Ala
 130 135 140
 Ile Val Thr Pro Gln Val Lys Gln Glu His Pro His Thr Asp Ser Asp
 145 150 155 160
 Leu Met His Val Lys Pro Gln His Glu Gln Arg Lys Glu Gln Glu Pro
 165 170 175
 Lys Arg Pro His Ile Lys Lys Pro Leu Asn Ala Phe Met Leu Tyr Met
 180 185 190
 Lys Glu Met Arg Ala Asn Val Val Ala Glu Cys Thr Leu Lys Glu Ser
 195 200 205
 Ala Ala Ile Asn Gln Ile Leu Gly Arg Arg Trp His Ala Leu Ser Arg
 210 215 220
 Glu Glu Gln Ala Lys Tyr Tyr Glu Leu Ala Arg Lys Glu Arg Gln Leu
 225 230 235 240
 His Met Gln Leu Tyr Pro Gly Trp Ser Ala Arg Asp Asn Tyr Gly Lys
 245 250 255
 Lys Lys Lys Arg Lys Arg Glu Lys Leu Gln Glu Ser Ala Ser Gly Thr
 260 265 270
 Gly Pro Arg Met Thr Ala Ala Tyr Ile
 275 280

715

<210> 773

<211> 195

<212> PRT

<213> Homo sapiens

<400> 773

Lys Ile Pro Phe Leu Gly Val Cys Leu Gly Met Gln Leu Ala Val Ile
1 5 10 15

Glu Phe Ala Arg Asn Cys Leu Asn Leu Lys Asp Ala Asp Ser Thr Glu
20 25 30

Phe Arg Pro Asn Ala Pro Val Pro Leu Val Ile Asp Met Pro Glu His
35 40 45

Asn Pro Gly Asn Leu Gly Gly Thr Met Arg Leu Gly Ile Arg Arg Thr
50 55 60

Val Phe Lys Thr Glu Asn Ser Ile Leu Arg Lys Leu Tyr Gly Asp Val
65 70 75 80

Pro Phe Ile Glu Glu Arg His Arg His Arg Phe Glu Val Asn Pro Asn
85 90 95

Leu Ile Lys Gln Phe Glu Gln Asn Asp Leu Ser Phe Val Gly Gln Asp
100 105 110

Val Asp Gly Asp Arg Met Glu Ile Ile Glu Leu Ala Asn His Pro Tyr
115 120 125

Phe Val Gly Val Gln Phe His Pro Glu Phe Ser Ser Arg Pro Met Lys
130 135 140

Pro Ser Pro Pro Tyr Leu Gly Leu Leu Leu Ala Ala Thr Gly Asn Leu
145 150 155 160

Asn Ala Tyr Leu Gln Gln Gly Cys Lys Leu Ser Ser Ser Asp Arg Tyr
165 170 175

Ser Asp Ala Ser Asp Asp Ser Phe Ser Glu Pro Arg Ile Ala Glu Leu
180 185 190

Glu Ile Ser
195

<210> 774

<211> 90

716

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (77)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 774

Glu Lys Gly Pro Ser Val Ser Val Lys Pro Lys Ala Gly Phe Cys Leu
1 5 10 15

Ala Gly Leu Arg Ser Gly Thr His Ser Trp Thr Asn His Asp Ile Pro
20 25 30

Asp Gly Val Thr Trp Pro Thr Cys Arg Lys Gly Val Gly Ser Val Pro
35 40 45

Glu Asp Arg Arg Gly Gly Val Gln Ile Gly Gln Glu Val Met Ala Ser
50 55 60

Gln Ala Pro Asn Cys Cys Asn Pro Gly Gly Gln Pro Xaa Val Glu Thr
65 70 75 80

Thr Gly Phe Arg Ala Val Pro Leu Pro Ser
85 90

<210> 775

<211> 205

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (12)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (110)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (131)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (138)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (141)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 775

Ser Cys Arg Ser Thr Leu Val Asp Pro Lys Lys Xaa Gly Thr Arg Glu
 1 5 10 15

Trp Gln Gln Val Asp Arg Gln Leu Pro Ser Leu Ala Cys Lys Tyr Pro
 20 25 30

Val Ser Ser Arg Glu Ala Thr Gln Ile Leu Ser Val Pro Lys Val Asp
 35 40 45

Asp Glu Ile Leu Gly Phe Ile Ser Glu Ala Thr Pro Leu Gly Gly Ile
 50 55 60

Gln Ala Ala Ser Thr Glu Ser Cys Asn Gln Gln Leu Asp Leu Ala Leu
 65 70 75 80

Cys Arg Ala Tyr Glu Ala Ala Ala Ser Ala Leu Gln Ile Ala Thr His
 85 90 95

Thr Ala Phe Val Ala Lys Ala Met Gln Ala Asp Ile Ser Xaa Ala Ala
 100 105 110

Gln Ile Leu Ser Ser Asp Pro Ser Arg Thr His Gln Ala Leu Gly Ile
 115 120 125

Leu Ser Xaa Thr Tyr Asp Ala Ala Ser Xaa Ile Cys Xaa Ala Ala Phe
 130 135 140

Asp Glu Val Lys Met Ala Ala His Thr Met Gly Asn Ala Thr Val Gly
 145 150 155 160

Arg Arg Tyr Leu Trp Leu Lys Asp Cys Lys Ile Asn Leu Ala Ser Lys
 165 170 175

Asn Lys Leu Ala Ser Thr Pro Phe Lys Gly Gly Thr Leu Phe Gly Gly
 180 185 190

Glu Val Cys Lys Val Ile Lys Lys Arg Gly Asn Lys His
 195 200 205

<210> 776

718

<211> 99
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (7)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 776
 Phe Ser Thr Arg Pro Ile Xaa Leu Thr Leu Met Leu Met Ala Val Leu
 1 5 10 15
 Asn Cys Leu Phe Asp Ser Leu Ser Gln Met Leu Arg Lys Asn Val Glu
 20 25 30
 Lys Arg Ala Leu Leu Glu Asn Met Glu Gly Leu Phe Leu Ala Val Asp
 35 40 45
 Glu Ile Val Asp Gly Gly Val Ile Leu Glu Ser Asp Pro Gln Gln Val
 50 55 60
 Val His Arg Val Ala Leu Arg Gly Glu Asp Val Pro Leu Thr Glu Gln
 65 70 75 80
 Thr Val Ser Gln Val Leu Gln Ser Ala Lys Glu Gln Ile Lys Trp Ser
 85 90 95
 Leu Leu Arg

<210> 777
 <211> 211
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (10)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (137)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 777
 Leu Gly Asp Thr Ile Glu Gly Thr Pro Xaa Gly Thr Gly Ser Gly Ile
 1 5 10 15

Pro Gly Ser Thr His Ala Ser Arg Glu Glu Lys Ser Lys Gln Phe Leu
20 25 30

Asp Leu Met Glu Thr Ile Asp Lys Gln Arg Glu Glu Met Ala Lys Ser
35 40 45

Ser Arg Ala Ser Ala Ala Arg Val Gly Lys Leu Gln Glu Ala Leu Asn
50 55 60

Glu Arg His Ser Ile Ile Asn Ala Leu Lys Ala Lys Leu Gln Met Thr
65 70 75 80

Glu Ala Ala Leu Ala Leu Ser Glu Gln Lys Ala Gln Asp Leu Gly Glu
85 90 95

Leu Leu Ala Thr Ala Glu Gln Glu Gln Leu Ser Leu Ser Gln Arg Gln
100 105 110

Ala Lys Glu Leu Lys Leu Glu Gln Gln Glu Ala Ala Glu Arg Glu Ser
115 120 125

Lys Leu Leu Arg Asp Leu Ser Ala Xaa Asn Glu Lys Asn Leu Leu Leu
130 135 140

Gln Asn Gln Val Asp Glu Leu Glu Arg Lys Phe Arg Cys Gln Gln Glu
145 150 155 160

Gln Leu Phe Gln Thr Arg Gln Glu Met Thr Ser Met Ser Ala Glu Leu
165 170 175

Lys Met Arg Ala Ile Gln Ala Arg Ser Ala Trp Thr Trp Arg Arg Glu
180 185 190

Asp Ala Asp Arg Ala Trp Arg Thr Pro Lys Ala Cys Ala Ser Arg Arg
195 200 205

Trp Ser Ile
210

<210> 778

<211> 181

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (145)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (155)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (163)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (169)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 778

Gly	Arg	Gly	Gly	Ala	Gly	Arg	Gly	Val	Pro	Leu	Val	Gly	Ser	Gly	Pro
1				5					10					15	

Arg	Ile	Leu	Ser	Ala	Gly	Ser	Arg	Arg	Pro	Arg	Ser	Cys	Ala	Pro	Pro
			20					25					30		

Pro	Gly	Pro	Gly	Leu	Gly	Arg	Val	Pro	Arg	Val	Leu	Gly	Ser	Phe	Cys
		35					40					45			

Pro	Pro	Val	Leu	Gln	Arg	Ser	Arg	Phe	Gln	Pro	Gly	Cys	Pro	Arg	Met
		50				55					60				

Gly	Glu	Phe	Asn	Glu	Lys	Lys	Thr	Thr	Cys	Gly	Thr	Val	Cys	Leu	Lys
65					70					75					80

Tyr	Leu	Leu	Phe	Thr	Tyr	Asn	Cys	Cys	Phe	Trp	Leu	Ala	Gly	Leu	Ala
				85						90				95	

Val	Met	Ala	Val	Gly	Ile	Trp	Thr	Leu	Ala	Leu	Lys	Ser	Asp	Tyr	Ile
			100					105						110	

Ser	Leu	Leu	Ala	Ser	Gly	Thr	Tyr	Leu	Ala	Thr	Ala	Tyr	Ile	Leu	Val
			115					120					125		

Val	Ala	Gly	Thr	Val	Val	Met	Val	Thr	Gly	Val	Leu	Gly	Cys	Cys	Ala
		130				135					140				

Xaa	Phe	Lys	Glu	Arg	Arg	Asn	Leu	Leu	Arg	Xaa	Tyr	Phe	Ile	Leu	Leu
145						150				155					160

Leu	Ile	Xaa	Phe	Leu	Ala	Gly	Asp	Xaa	Arg	Trp	Tyr	Pro	Arg	Leu	Arg
				165					170					175	

Leu Ile Thr Ser Ser

180

<210> 779

<211> 132

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 779

Ser Arg Ala Lys Arg Xaa Pro Lys Ser Lys Glu Leu Val Ser Ser Ser
 1 5 10 15

Ser Ser Gly Ser Asp Ser Asp Ser Glu Val Asp Lys Lys Leu Lys Arg
 20 25 30

Lys Lys Gln Val Ala Pro Glu Lys Pro Val Lys Lys Gln Lys Thr Gly
 35 40 45

Glu Thr Ser Arg Ala Leu Ser Ser Ser Lys Gln Ser Ser Ser Ser Arg
 50 55 60

Asp Asp Asn Met Phe Gln Ile Gly Lys Met Arg Tyr Val Ser Val Arg
 65 70 75 80

Asp Phe Lys Gly Lys Val Leu Ile Asp Ile Arg Glu Tyr Trp Met Asp
 85 90 95

Pro Glu Gly Glu Met Lys Pro Gly Arg Lys Gly Ile Ser Leu Asn Pro
 100 105 110

Glu Gln Trp Ser Gln Leu Lys Glu Gln Ile Ser Asp Ile Asp Asp Ala
 115 120 125

Val Arg Lys Leu
 130

<210> 780

<211> 370

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (39)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (56)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 780

Asp	Asn	Lys	Lys	Tyr	Glu	Ile	Ile	Lys	Arg	Asp	Ile	Leu	Arg	Gly	Lys
1				5				10						15	

Ser	Val	Pro	His	Tyr	Ala	Ala	Ile	Glu	Pro	Asp	Gly	Asn	Gly	Leu	Met
			20					25						30	

Ile	Val	Ser	Tyr	Lys	Ser	Xaa	Thr	Phe	Val	Gln	Ala	Gly	Gln	Asp	Leu
		35					40					45			

Glu	Glu	Asn	Met	Asp	Glu	Asp	Xaa	Ser	Glu	Lys	Ile	Lys	Glu	Pro	Leu
	50					55					60				

Tyr	Tyr	Trp	Gln	Gln	Thr	Glu	Asp	Asp	Leu	Thr	Val	Thr	Ile	Arg	Leu
65					70				75						80

Pro	Glu	Asp	Ser	Thr	Lys	Glu	Asp	Ile	Gln	Ile	Gln	Phe	Leu	Pro	Asp
			85						90					95	

His	Ile	Asn	Ile	Val	Leu	Lys	Asp	His	Gln	Phe	Leu	Glu	Gly	Lys	Leu
			100					105					110		

Tyr	Ser	Ser	Ile	Asp	His	Glu	Ser	Ser	Thr	Trp	Ile	Ile	Lys	Glu	Ser
		115					120						125		

Asn	Ser	Leu	Glu	Ile	Ser	Leu	Ile	Lys	Lys	Asn	Glu	Gly	Leu	Thr	Trp
	130					135					140				

Pro	Glu	Leu	Val	Ile	Gly	Asp	Lys	Gln	Gly	Glu	Leu	Ile	Arg	Asp	Ser
145					150					155					160

Ala	Gln	Cys	Ala	Ala	Ile	Ala	Glu	Arg	Leu	Met	His	Leu	Thr	Ser	Glu
			165						170					175	

Glu	Leu	Asn	Pro	Asn	Pro	Asp	Lys	Glu	Lys	Pro	Pro	Cys	Asn	Ala	Gln
		180						185					190		

Glu	Leu	Glu	Glu	Cys	Asp	Ile	Phe	Phe	Glu	Glu	Ser	Ser	Ser	Leu	Cys
	195						200					205			

Arg	Phe	Asp	Gly	Asn	Thr	Leu	Lys	Thr	Thr	His	Val	Val	Asn	Leu	Gly
	210					215					220				

723

Ser Asn Gln Tyr Leu Phe Ser Val Ile Val Asp Pro Lys Glu Met Pro
225 230 235 240

Cys Phe Cys Leu Arg His Asp Val Asp Ala Leu Leu Trp Gln Pro His
 245 250 255

Ser Ser Lys Gln Asp Asp Met Trp Glu His Ile Ala Thr Phe Asn Ala
 260 265 270

Leu Gly Tyr Val Gln Ala Ser Lys Arg Asp Lys Lys Phe Phe Ala Cys
 275 280 285

Ala Pro Asn Tyr Ser Tyr Ala Ala Leu Cys Glu Cys Leu Arg Arg Val
 290 295 300

Phe Ile Tyr Arg Gln Pro Ala Pro Met Ser Thr Val Leu Tyr Asn Arg
305 310 315 320

Lys Glu Gly Arg Gln Val Gly Gln Val Ala Lys Gln Gln Val Ala Ser
 325 330 335

Leu Glu Thr Asn Asp Pro Ile Leu Gly Phe Gln Ala Thr Asn Glu Arg
 340 345 350

Leu Phe Val Leu Thr Thr Lys Asn Leu Phe Leu Ile Lys Val Asn Thr
 355 360 365

Glu Asn
 370

<210> 781
<211> 259
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (215)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (227)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (228)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (247)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (251)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (257)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (259)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 781

Gly Gly Asp Pro Gly Gly Gly Gly Arg Ser Pro Ala Leu Arg Gln Lys

1

5

10

15

Val Pro Arg Leu His Thr Arg Ala Arg Ser Gln Arg Ala Ala Gly Ala

20

25

30

Asp Gly Arg Arg Gly Gly Arg Arg Gln Gly Arg Ser Val Tyr Ser Cys

35

40

45

Ser Gly Ala Val Ser Trp Arg Arg Leu Gly Arg Leu Leu Ser Pro Gly

50

55

60

Ser Ala Ala Ala Ala Lys Ala Ala Ala Pro Ala Leu Ser Leu Ser Leu

65

70

75

80

Ser Arg Leu Trp Leu Gln Val Lys Gly Lys Gln Ala Arg Met Asp Ile

85

90

95

Tyr Asp Thr Gln Thr Leu Gly Val Val Val Phe Gly Gly Phe Met Val

100

105

110

Val Ser Ala Ile Gly Ile Phe Leu Val Ser Thr Phe Ser Met Lys Glu

115

120

125

Thr Ser Tyr Glu Glu Ala Leu Ala Asn Gln Arg Lys Glu Met Ala Lys

130

135

140

Thr His His Gln Lys Val Glu Lys Lys Lys Lys Glu Lys Thr Val Glu

145

150

155

160

Lys Lys Gly Lys Thr Lys Lys Lys Glu Glu Lys Pro Asn Gly Lys Ile
 165 170 175
 Pro Asp His Asp Pro Ala Pro Asn Val Thr Val Leu Leu Arg Glu Pro
 180 185 190
 Val Arg Ala Pro Ala Val Ala Val Ala Pro Thr Pro Val Gln Pro Pro
 195 200 205
 Ile Ile Val Ala Pro Val Xaa Thr Val Pro Ala Met Pro Gln Glu Lys
 210 215 220
 Leu Ala Xaa Xaa Pro Lys Asp Lys Lys Lys Lys Glu Lys Lys Val Ala
 225 230 235 240
 Lys Val Gly Pro Val Ser Xaa Cys Ser Asp Xaa Ile Gln Val Ser Ile
 245 250 255
 Xaa Lys Xaa

<210> 782
 <211> 177
 <212> PRT
 <213> Homo sapiens

<400> 782
 Gly Ser Pro Val Glu Pro Arg Gly Ser Ala Pro Glu Ile Met Leu Asn
 1 5 10 15
 Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile
 20 25 30
 Leu Ala Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr
 35 40 45
 Leu Asp Gln Leu Asn His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln
 50 55 60
 Glu Asp Leu Asn Cys Ile Ile Asn Met Lys Ala Arg Asn Tyr Leu Gln
 65 70 75 80
 Ser Leu Pro Ser Lys Thr Lys Val Ala Trp Ala Lys Leu Phe Pro Lys
 85 90 95
 Ser Asp Ser Lys Ala Leu Asp Leu Leu Asp Arg Met Leu Thr Phe Asn
 100 105 110

Pro Asn Lys Arg Ile Thr Val Glu Glu Ala Leu Ala His Pro Tyr Leu
 115 120 125

Glu Gln Tyr Tyr Asp Pro Thr Asp Glu Pro Val Ala Glu Glu Pro Phe
 130 135 140

Thr Phe Ala Met Glu Leu Asp Asp Leu Pro Lys Glu Arg Leu Lys Glu
 145 150 155 160

Leu Ile Phe Gln Glu Thr Ala Arg Phe Gln Pro Gly Val Leu Glu Ala
 165 170 175

Pro

<210> 783

<211> 154

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (153)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 783

His Leu Tyr Ala Phe Phe Ile Gln Trp Ser Pro Glu Ile Tyr Ala Glu
 1 5 10 15

Asp Thr Gly Glu Tyr Thr Arg Glu Pro Gly Phe Ile Val Val Lys Lys
 20 25 30

Ile Glu Glu Ser Glu Thr Ile Glu Asp Ser Ser Asn Gln Ala Ala Ala
 35 40 45

Arg Glu Trp Glu Ile Thr Thr Arg Glu Asp Ile Asn Ser Lys Gln Val
 50 55 60

Ala Thr Val Lys Ala Asp Leu Glu Ser Glu Ser Phe Arg Pro Asn Leu
 65 70 75 80

Ser Asp Pro Ser Glu Leu Leu Leu Pro Asp Gln Ile Glu Lys Leu Thr
 85 90 95

Lys His Leu Pro Pro Arg Thr Ile Gly Tyr Pro Trp Thr Leu Val Tyr
 100 105 110

Gly Thr Gly Lys His Gly Thr Ser Leu Lys Thr Leu Tyr Arg Thr Met
 115 120 125

Thr Gly Leu Asp Thr Pro Val Leu Met Val Ile Lys Asp Ser Asp Gly
 130 135 140

Gln Val Phe Gly Ala Leu His Leu Xaa His
 145 150

<210> 784

<211> 164

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (48)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (118)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (130)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 784

Phe Leu Tyr Ser Phe Ala Arg Gln Thr Met Ala Pro Phe Gly Arg Asn
 1 5 10 15

Leu Leu Lys Thr Arg His Lys Asn Arg Ser Pro Thr Lys Asp Met Asp
 20 25 30

Ser Glu Glu Lys Glu Ile Val Val Trp Val Cys Gln Glu Glu Lys Xaa
 35 40 45

Val Cys Gly Leu Thr Lys Arg Thr Thr Ser Ala Asp Val Ile Gln Ala
 50 55 60

Leu Leu Glu Glu His Glu Ala Thr Phe Gly Glu Lys Arg Phe Leu Leu
 65 70 75 80

Gly Lys Pro Ser Asp Tyr Cys Ile Ile Glu Lys Trp Arg Gly Ser Glu
 85 90 95

Arg Val Leu Pro Pro Leu Thr Arg Ile Leu Lys Leu Trp Lys Ala Trp
 100 105 110

728

Gly Asp Glu Gln Pro Xaa Met Gln Phe Val Leu Val Lys Ala Asp Ala
 115 120 125

Phe Xaa Pro Val Pro Leu Trp Arg Thr Ala Glu Ala Lys Leu Val Gln
 130 135 140

Asn Thr Glu Lys Leu Trp Glu Leu Ser Pro Ala Asn Leu His Glu Asp
 145 150 155 160

Phe Thr Thr Arg

<210> 785

<211> 72

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (68)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 785

Gly Tyr Arg Leu Ser Cys Glu Val Ile Ser Ile Trp Lys Gln Val Trp
 1 5 10 15

Gly Ala Gly Gly Ala Leu Val Arg Val Leu Gly Gly Ser Gly Val Ser
 20 25 30

Val Gly Gly Ser Thr Gly Tyr Thr Gly Ala Arg Lys Glu His Gly Val
 35 40 45

Thr Cys Ser Val Gly Val Arg Leu Gly Val Gln Val Glu Glu Pro Gly
 50 55 60

Val Leu Gly Xaa Gln Ser Val Xaa
 65 70

<210> 786

<211> 332

<212> PRT

<213> Homo sapiens

<220>
 <221> SITE
 <222> (37)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (298)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (303)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (323)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 786

Gly Lys Gln Arg Glu Gly Arg Arg Glu Gly Ile Arg Gln Leu Gln Phe
 1 5 10 15

Ser Ser Leu Gly Ala Pro Thr Pro Arg Cys Pro Ala Ser Cys Pro Gln
 20 25 30

Pro Gly His Ala Xaa Pro Thr Leu Pro Ala Pro Gln Asn Pro Arg His
 35 40 45

Pro Pro Glu Pro Pro Gln Ser Trp Pro Arg Arg Met Gly Ala Leu Arg
 50 55 60

Pro Thr Leu Leu Pro Pro Ser Leu Pro Leu Leu Leu Leu Met Leu
 65 70 75 80

Gly Met Gly Cys Trp Ala Arg Glu Val Leu Val Pro Glu Gly Pro Leu
 85 90 95

Tyr Arg Val Ala Gly Thr Ala Val Ser Ile Ser Cys Asn Val Thr Gly
 100 105 110

Tyr Glu Gly Pro Ala Gln Gln Asn Phe Glu Trp Phe Leu Tyr Arg Pro
 115 120 125

Glu Ala Pro Asp Thr Ala Leu Gly Ile Val Ser Thr Lys Asp Thr Gln
 130 135 140

Phe Ser Tyr Ala Val Phe Lys Ser Arg Val Val Ala Gly Glu Val Gln
 145 150 155 160

730

Val Gln Arg Leu Gln Gly Asp Ala Val Val Leu Lys Ile Ala Arg Leu
 165 170 175
 Gln Ala Gln Asp Ala Gly Ile Tyr Glu Cys His Thr Pro Ser Thr Asp
 180 185 190
 Thr Arg Tyr Leu Gly Ser Tyr Ser Gly Lys Val Glu Leu Arg Val Leu
 195 200 205
 Pro Asp Val Leu Gln Val Ser Ala Ala Pro Pro Gly Pro Arg Gly Arg
 210 215 220
 Gln Ala Pro Thr Ser Pro Pro Arg Met Thr Val His Glu Gly Gln Glu
 225 230 235 240
 Leu Ala Leu Gly Cys Leu Ala Arg Thr Ser Thr Gln Lys His Thr His
 245 250 255
 Leu Ala Val Ser Phe Gly Arg Ser Val Pro Glu Ala Pro Val Gly Arg
 260 265 270
 Ser Thr Leu Gln Glu Val Val Gly Ile Arg Ser Asp Leu Ala Val Glu
 275 280 285
 Ala Gly Ala Pro Tyr Ala Glu Arg Leu Xaa Ala Gly Glu Leu Xaa Leu
 290 295 300
 Gly Lys Glu Gly Thr Asp Arg Tyr Arg Met Val Val Gly Gly Ala Gln
 305 310 315 320
 Ala Gly Xaa Arg Arg His Leu Pro Leu His Cys Arg
 325 330

<210> 787

<211> 576

<212> PRT

<213> Homo sapiens

<400> 787

Glu Lys Glu Thr Ala Gln Leu Arg Glu Gln Val Gly Arg Met Glu Arg
 1 5 10 15
 Glu Leu Asn His Glu Lys Glu Arg Cys Asp Gln Leu Gln Ala Glu Gln
 20 25 30
 Lys Gly Leu Thr Glu Val Thr Gln Ser Leu Lys Met Glu Asn Glu Glu
 35 40 45

731

Phe Lys Lys Arg Phe Ser Asp Ala Thr Ser Lys Ala His Gln Leu Glu
 50 55 60

Glu Asp Ile Val Ser Val Thr His Lys Ala Ile Glu Lys Glu Thr Glu
 65 70 75 80

Leu Asp Ser Leu Lys Asp Lys Leu Lys Lys Ala Gln His Glu Arg Glu
 85 90 95

Gln Leu Glu Cys Gln Leu Lys Thr Glu Lys Asp Glu Lys Glu Leu Tyr
 100 105 110

Lys Val His Leu Lys Asn Thr Glu Ile Glu Asn Thr Lys Leu Met Ser
 115 120 125

Glu Val Gln Thr Leu Lys Asn Leu Asp Gly Asn Lys Glu Ser Val Ile
 130 135 140

Thr His Phe Lys Glu Glu Ile Gly Arg Leu Gln Leu Cys Leu Ala Glu
 145 150 155 160

Lys Glu Asn Leu Gln Arg Thr Phe Leu Leu Thr Thr Ser Ser Lys Glu
 165 170 175

Asp Thr Cys Phe Leu Lys Glu Gln Leu Arg Lys Ala Glu Glu Gln Val
 180 185 190

Gln Ala Thr Arg Gln Glu Val Val Phe Leu Ala Lys Glu Leu Ser Asp
 195 200 205

Ala Val Asn Val Arg Asp Arg Thr Met Ala Asp Leu His Thr Ala Arg
 210 215 220

Leu Glu Asn Glu Lys Val Lys Lys Gln Leu Ala Asp Ala Val Ala Glu
 225 230 235 240

Leu Lys Leu Asn Ala Met Lys Lys Asp Gln Asp Lys Thr Asp Thr Leu
 245 250 255

Glu His Glu Leu Arg Arg Glu Val Glu Asp Leu Lys Leu Arg Leu Gln
 260 265 270

Met Ala Ala Asp His Tyr Lys Glu Lys Phe Lys Glu Cys Gln Arg Leu
 275 280 285

Gln Lys Gln Ile Asn Lys Leu Ser Asp Gln Ser Ala Asn Asn Asn Asn
 290 295 300

Val Phe Thr Lys Lys Thr Gly Asn Gln Gln Lys Val Asn Asp Ala Ser
 305 310 315 320

Val Asn Thr Asp Pro Ala Thr Ser Ala Ser Thr Val Asp Val Lys Pro
 325 330 335
 Ser Pro Ser Ala Ala Glu Ala Asp Phe Asp Ile Val Thr Lys Gly Gln
 340 345 350
 Val Cys Glu Met Thr Lys Glu Ile Ala Asp Lys Thr Glu Lys Tyr Asn
 355 360 365
 Lys Cys Lys Gln Leu Leu Gln Asp Glu Lys Ala Lys Cys Asn Lys Tyr
 370 375 380
 Ala Asp Glu Leu Ala Lys Met Glu Leu Lys Trp Lys Glu Gln Val Lys
 385 390 395 400
 Ile Ala Glu Asn Val Lys Leu Glu Leu Ala Glu Val Gln Asp Asn Tyr
 405 410 415
 Lys Glu Leu Lys Arg Ser Leu Glu Asn Pro Ala Glu Arg Lys Met Glu
 420 425 430
 Asp Gly Ala Asp Gly Ala Phe Tyr Pro Asp Glu Ile Gln Arg Pro Pro
 435 440 445
 Val Arg Val Pro Ser Trp Gly Leu Glu Asp Asn Val Val Cys Ser Gln
 450 455 460
 Pro Ala Arg Asn Phe Ser Arg Pro Asp Gly Leu Glu Asp Ser Glu Asp
 465 470 475 480
 Ser Lys Glu Asp Glu Asn Val Pro Thr Ala Pro Asp Pro Pro Ser Gln
 485 490 495
 His Leu Arg Gly His Gly Thr Gly Phe Cys Phe Asp Ser Ser Phe Asp
 500 505 510
 Val His Lys Lys Cys Pro Leu Cys Glu Leu Met Phe Pro Pro Asn Tyr
 515 520 525
 Asp Gln Ser Lys Phe Glu Glu His Val Glu Ser His Trp Lys Val Cys
 530 535 540
 Pro Met Cys Ser Glu Gln Phe Pro Pro Asp Tyr Asp Gln Gln Val Phe
 545 550 555 560
 Glu Arg His Val Gln Thr His Phe Asp Gln Asn Val Leu Asn Phe Asp
 565 570 575

<210> 788
 <211> 311
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (135)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (175)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 788

Ala	Ile	Val	Pro	Ser	Trp	Asp	Leu	Asp	Lys	Asp	Thr	Ile	Ser	Leu	Leu
1				5					10					15	
Ser	Pro	Val	Leu	Cys	Ile	Phe	Pro	Ser	Pro	Ser	Ser	Gln	Thr	Ser	Leu
			20					25					30		
Leu	Tyr	Val	Phe	Ser	Leu	Ala	Gly	Arg	Met	Thr	Gln	Asn	Thr	Val	Ile
	35						40					45			
Val	Asn	Gly	Val	Ala	Met	Ala	Ser	Arg	Pro	Ser	Gln	Pro	Thr	His	Val
	50					55					60				
Asn	Val	His	Ile	His	Gln	Glu	Ser	Ala	Leu	Thr	Gln	Leu	Leu	Lys	Ala
65					70					75				80	
Gly	Gly	Ser	Leu	Lys	Lys	Phe	Leu	Phe	His	Pro	Gly	Asp	Thr	Val	Pro
			85						90					95	
Ser	Thr	Ala	Arg	Ile	Gly	Tyr	Glu	Gln	Leu	Ala	Leu	Gly	Val	Thr	Gln
		100						105					110		
Ile	Leu	Leu	Gly	Val	Val	Ser	Cys	Val	Leu	Gly	Val	Cys	Leu	Ser	Leu
	115						120					125			
Gly	Pro	Trp	Thr	Val	Leu	Xaa	Ala	Ser	Gly	Cys	Ala	Phe	Trp	Ala	Gly
	130					135					140				
Ser	Val	Val	Ile	Ala	Ala	Gly	Ala	Gly	Ala	Ile	Val	His	Glu	Lys	His
145					150					155				160	
Pro	Gly	Lys	Leu	Ala	Gly	Tyr	Ile	Ser	Ser	Leu	Leu	Thr	Leu	Xaa	Gly
			165						170					175	

734

Phe Ala Thr Ala Met Ala Ala Val Val Leu Cys Val Asn Ser Phe Ile
180 185 190

Trp Gln Thr Glu Pro Phe Leu Tyr Ile Asp Thr Val Cys Asp Arg Ser
195 200 205

Asp Pro Val Phe Pro Thr Thr Gly Tyr Arg Trp Met Arg Arg Ser Gln
210 215 220

Glu Asn Gln Trp Gln Lys Glu Glu Cys Arg Ala Tyr Met Gln Met Leu
225 230 235 240

Arg Lys Leu Phe Thr Ala Ile Arg Ala Leu Phe Leu Ala Val Cys Val
245 250 255

Leu Lys Val Ile Val Ser Leu Val Ser Leu Gly Val Gly Leu Arg Asn
260 265 270

Leu Cys Gly Gln Ser Ser Gln Pro Leu Asn Glu Glu Gly Ser Glu Lys
275 280 285

Arg Leu Leu Gly Glu Asn Ser Val Pro Pro Ser Pro Ser Arg Glu Gln
290 295 300

Thr Ser Thr Ala Ile Val Leu
305 310

<210> 789

<211> 76

<212> PRT

<213> Homo sapiens

<400> 789

His Ser Lys Ser Phe Val Leu Phe Lys Ile Cys Phe Gly Asn Tyr His
1 5 10 15

Ile Phe Phe Ser Tyr Leu Pro Leu Asn Gly His Ser Val Tyr Cys Trp
20 25 30

Asn Val Pro Ser Lys Arg Cys Ser Phe Arg Ser Thr Val Ile Ala Pro
35 40 45

Gly Ser Met Arg Tyr Cys Leu Tyr Tyr Glu Val Gly Val Leu Ser Thr
50 55 60

Glu Ile Ile Leu Leu Asn Lys Tyr Val Cys Ser Val
65 70 75

735

<210> 790
<211> 106
<212> PRT
<213> Homo sapiens

<400> 790
Ala Ser Ser Ala Cys Leu Ala Ala Pro Ala Leu Ser Arg Leu Pro Gly
1 5 10 15
Leu Gly Gly Ala Gly Ala Arg Ser Arg Ser Cys Leu Gly Leu Arg Phe
20 25 30
Gln Ala Trp Gly Ser Leu Pro Ala Ala Arg Ser Arg Ala Val Leu Gly
35 40 45
Thr Leu Arg Ser Thr Glu Pro Ser Leu Thr Gln Glu Leu Ser Ala Asp
50 55 60
Ser Pro Pro Ser Gly Ser Glu Ala Thr Trp Met Gln Ser Ala Lys Ser
65 70 75 80
Pro Trp Lys Ser Cys Phe Pro Ser Thr Ser Trp Ile Ser Gly Leu Leu
85 90 95
Ser Ser Ser Ser Trp Pro Pro Leu Ser Ser
100 105

<210> 791
<211> 121
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 791
Ser Glu Lys Ser Thr Glu His Pro Glu Lys Thr Xaa Ala Thr Thr Glu
1 5 10 15
Lys Thr Thr Arg Thr Pro Glu Lys Pro Thr Leu Tyr Ser Glu Lys Thr
20 25 30
Ile Cys Thr Lys Gly Lys Asn Thr Pro Val Pro Glu Lys Pro Thr Glu
35 40 45
Asn Leu Gly Asn Thr Thr Leu Thr Thr Glu Thr Ile Lys Ala Pro Val

736

50 55 60
 Lys Ser Thr Glu Asn Pro Glu Lys Thr Ala Ala Val Thr Lys Thr Ile
 65 70 75 80
 Lys Pro Ser Val Lys Val Thr Gly Asp Lys Ser Leu Thr Thr Thr Ser
 85 90 95
 Ser His Leu Asn Lys Thr Glu Val Thr His Gln Val Pro Thr Gly Ser
 100 105 110
 Phe Thr Leu Ile Thr Ser Arg Thr Ser
 115 120

<210> 792
 <211> 128
 <212> PRT
 <213> Homo sapiens

<400> 792
 Gln Thr Ala Thr Phe Gln Gly Ala Thr Thr Val Gly Gly Ser Lys Glu
 1 5 10 15
 Arg Lys Glu Lys Arg Arg Gln Arg Lys Gly Glu Glu Cys Ser Leu Pro
 20 25 30
 Gly Leu Thr Cys Phe Thr His Asp Asn Asn His Trp Gln Thr Ala Pro
 35 40 45
 Phe Trp Asn Leu Gly Ser Phe Cys Ala Cys Thr Ser Ser Asn Asn Asn
 50 55 60
 Thr Tyr Trp Cys Leu Arg Thr Val Asn Glu Thr His Asn Phe Leu Phe
 65 70 75 80
 Cys Glu Phe Ala Thr Gly Phe Leu Glu Tyr Phe Asp Met Asn Thr Asp
 85 90 95
 Pro Tyr Gln Leu Thr Asn Thr Val His Thr Val Glu Arg Gly Ile Leu
 100 105 110
 Asn Gln Leu His Val Gln Leu Met Gly Ala Gln Lys Leu Ser Arg Val
 115 120 125

737

<210> 793

<211> 190

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 793

Asp Pro Xaa Val Arg Ser Gln Lys Lys Lys Lys Lys Met Ser Ser Trp
 1 5 10 15

Pro Tyr Phe Gln Pro Phe Asp Ser Leu Ser Thr Ser Leu Val Leu Val
 20 25 30

Cys Leu Cys Gln Arg His Val Arg His Leu Gln Arg Asp Ala Leu Ser
 35 40 45

Gln Leu Met Asn Gly Pro Ile Arg Lys Lys Leu Lys Ile Ile Pro Glu
 50 55 60

Asp Gln Ser Trp Gly Gly Gln Ala Thr Asn Val Phe Val Asn Met Glu
 65 70 75 80

Glu Asp Phe Met Lys Pro Val Ile Ser Ile Val Asp Glu Leu Leu Glu
 85 90 95

Ala Gly Ile Asn Val Thr Val Tyr Asn Gly Gln Leu Asp Leu Ile Val
 100 105 110

Asp Thr Met Gly Gln Glu Ala Trp Val Arg Lys Leu Lys Trp Pro Glu
 115 120 125

Leu Pro Lys Phe Ser Gln Leu Lys Trp Lys Ala Leu Tyr Ser Asp Pro
 130 135 140

Lys Ser Leu Glu Thr Ser Ala Phe Val Lys Ser Tyr Lys Asn Leu Ala
 145 150 155 160

Phe Tyr Trp Ile Leu Lys Ala Gly His Met Val Pro Ser Asp Gln Gly
 165 170 175

Asp Met Ala Leu Lys Met Met Arg Leu Val Thr Gln Gln Glu
 180 185 190

<210> 794

<211> 260

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (106)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 794

Asn His Ser Cys Trp Gln Gly Pro Gln Leu Met Pro Ala Ser Ser Pro
 1 5 10 15

Phe Leu Leu Ala Pro Lys Gly Pro Pro Gly Asn Met Gly Gly Pro Val
 20 25 30

Arg Glu Pro Ala Leu Ser Val Ala Leu Trp Leu Ser Trp Gly Ala Ala
 35 40 45

Leu Gly Ala Val Ala Cys Ala Met Ala Leu Leu Thr Gln Gln Thr Glu
 50 55 60

Leu Gln Ser Leu Arg Arg Glu Val Ser Arg Leu Gln Gly Thr Gly Gly
 65 70 75 80

Pro Ser Gln Asn Gly Glu Gly Tyr Pro Trp Gln Ser Leu Pro Glu Gln
 85 90 95

Ser Ser Asp Ala Leu Glu Ala Trp Glu Xaa Gly Glu Arg Ser Arg Lys
 100 105 110

Arg Arg Ala Val Leu Thr Gln Lys Gln Lys Lys Gln His Ser Val Leu
 115 120 125

His Leu Val Pro Ile Asn Ala Thr Ser Lys Asp Asp Ser Asp Val Thr
 130 135 140

Glu Val Met Trp Gln Pro Ala Leu Arg Arg Gly Arg Gly Leu Gln Ala
 145 150 155 160

Gln Gly Tyr Gly Val Arg Ile Gln Asp Ala Gly Val Tyr Leu Leu Tyr
 165 170 175

Ser Gln Val Leu Phe Gln Asp Val Thr Phe Thr Met Gly Gln Val Val
 180 185 190

Ser Arg Glu Gly Gln Gly Arg Gln Glu Thr Leu Phe Arg Cys Ile Arg
 195 200 205

Ser Met Pro Ser His Pro Asp Arg Ala Tyr Asn Ser Cys Tyr Ser Ala
 210 215 220

Gly Val Phe His Leu His Gln Gly Asp Ile Leu Ser Val Ile Ile Pro
 225 230 235 240

Arg Ala Arg Ala Lys Leu Asn Leu Ser Pro His Gly Thr Phe Leu Gly
 245 250 255

Phe Val Lys Leu
 260

<210> 795

<211> 310

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 795

Gly Thr Arg Leu Arg Val Ala Leu Glu Ala Gln Ser Pro Arg Arg Arg
 1 5 10 15

Ala Gly Trp Cys Ser Cys Ala Gly Gly Val Leu Arg Leu Gly Val Val
 20 25 30

Thr Gly Ser Arg Met Ala Ser Asp Ser Gly Asn Gln Gly Thr Leu Cys
 35 40 45

Thr Leu Glu Phe Ala Val Gln Met Thr Cys Gln Ser Cys Val Asp Ala
 50 55 60

Val Arg Lys Ser Leu Gln Gly Xaa Ala Gly Val Gln Asp Val Glu Val
 65 70 75 80

His Leu Glu Asp Gln Met Val Leu Val His Thr Thr Leu Pro Ser Gln
 85 90 95

Glu Val Gln Ala Leu Leu Glu Gly Thr Gly Arg Gln Ala Val Leu Lys
 100 105 110

Gly Met Gly Ser Gly Gln Leu Gln Asn Leu Gly Ala Ala Val Ala Ile
 115 120 125

Leu Gly Gly Pro Gly Thr Val Gln Gly Val Val Arg Phe Leu Gln Leu
 130 135 140

Thr Pro Glu Arg Cys Leu Ile Glu Gly Thr Ile Asp Gly Leu Glu Pro
 145 150 155 160

740

Gly Leu His Gly Leu His Val His Gln Tyr Gly Asp Leu Thr Asn Asn
 165 170 175
 Cys Asn Ser Cys Gly Asn His Phe Asn Pro Asp Gly Ala Ser His Gly
 180 185 190
 Gly Pro Gln Asp Ser Asp Arg His Arg Gly Asp Leu Gly Asn Val Arg
 195 200 205
 Ala Asp Ala Asp Gly Arg Ala Ile Phe Arg Met Glu Asp Glu Gln Leu
 210 215 220
 Lys Val Trp Asp Val Ile Gly Arg Ser Leu Ile Ile Asp Glu Gly Glu
 225 230 235 240
 Asp Asp Leu Gly Arg Gly Gly His Pro Leu Ser Lys Ile Thr Gly Asn
 245 250 255
 Ser Gly Glu Arg Leu Ala Cys Gly Ile Ile Ala Arg Ser Ala Gly Leu
 260 265 270
 Phe Gln Asn Pro Lys Gln Ile Cys Ser Cys Asp Gly Leu Thr Ile Trp
 275 280 285
 Glu Glu Arg Gly Arg Pro Ile Ala Gly Lys Gly Arg Lys Glu Ser Ala
 290 295 300
 Gln Pro Pro Ala His Leu
 305 310

<210> 796

<211> 465

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (59)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 796

Ala Gly Glu Lys Leu Leu Lys Asp Cys Val Leu Leu His Leu Pro Cys
 1 5 10 15

Ala Arg Ser Pro Pro Val Ser His Ser Val Thr Met Val Gln Trp Lys
 20 25 30

Arg Leu Cys Gln Leu His Tyr Leu Trp Ala Leu Gly Cys Tyr Met Leu

741

35	40	45
Leu Ala Thr Val Ala Leu Lys Leu Ser Phe Xaa Leu Lys Cys Asp Ser		
50	55	60
Asp His Leu Gly Leu Glu Ser Arg Glu Ser Gln Ser Gln Tyr Cys Arg		
65	70	75
Asn Ile Leu Tyr Asn Phe Leu Lys Leu Pro Ala Lys Arg Ser Ile Asn		
85	90	95
Cys Ser Gly Val Thr Arg Gly Asp Gln Glu Ala Val Leu Gln Ala Ile		
100	105	110
Leu Asn Asn Leu Glu Val Lys Lys Lys Arg Glu Pro Phe Thr Asp Thr		
115	120	125
His Tyr Leu Ser Leu Thr Arg Asp Cys Glu His Phe Lys Ala Glu Arg		
130	135	140
Lys Phe Ile Gln Phe Pro Leu Ser Lys Glu Glu Val Glu Phe Pro Ile		
145	150	155
Ala Tyr Ser Met Val Ile His Glu Lys Ile Glu Asn Phe Glu Arg Leu		
165	170	175
Leu Arg Ala Val Tyr Ala Pro Gln Asn Ile Tyr Cys Val His Val Asp		
180	185	190
Glu Lys Ser Pro Glu Thr Phe Lys Glu Ala Val Lys Ala Ile Ile Ser		
195	200	205
Cys Phe Pro Asn Val Phe Ile Ala Ser Lys Leu Val Arg Val Val Tyr		
210	215	220
Ala Ser Trp Ser Arg Val Gln Ala Asp Leu Asn Cys Met Glu Asp Leu		
225	230	235
Leu Gln Ser Ser Val Pro Trp Lys Tyr Phe Leu Asn Thr Cys Gly Thr		
245	250	255
Asp Phe Pro Ile Lys Ser Asn Ala Glu Met Val Gln Ala Leu Lys Met		
260	265	270
Leu Asn Gly Arg Asn Ser Met Glu Ser Glu Val Pro Pro Lys His Lys		
275	280	285
Glu Thr Arg Trp Lys Tyr His Phe Glu Val Val Arg Asp Thr Leu His		
290	295	300
Leu Thr Asn Lys Lys Lys Asp Pro Pro Pro Tyr Asn Leu Thr Met Phe		

742

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305              310              315              320
Thr Gly Asn Ala Tyr Ile Val Ala Ser Arg Asp Phe Val Gln His Val
              325              330              335
Leu Lys Asn Pro Lys Ser Gln Gln Leu Ile Glu Trp Val Lys Asp Thr
              340              345              350
Tyr Ser Pro Asp Glu His Leu Trp Ala Thr Leu Gln Arg Ala Arg Trp
              355              360              365
Met Pro Gly Ser Val Pro Asn His Pro Lys Tyr Asp Ile Ser Asp Met
              370              375              380
Thr Ser Ile Ala Arg Leu Val Lys Trp Gln Gly His Glu Gly Asp Ile
385              390              395              400
Asp Lys Gly Ala Pro Tyr Ala Pro Cys Ser Gly Ile His Gln Arg Ala
              405              410              415
Ile Cys Val Tyr Gly Ala Gly Asp Leu Asn Trp Met Leu Gln Asn His
              420              425              430
His Leu Leu Ala Asn Lys Phe Asp Pro Lys Val Asp Asp Asn Ala Leu
              435              440              445
Gln Cys Leu Glu Glu Tyr Leu Arg Tyr Lys Ala Ile Tyr Gly Thr Glu
              450              455              460
Leu
465

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<210> 797

<211> 977

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (762)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 797

Gly Ser Leu Ser Arg Leu Pro Thr Ile Thr Met Ala Lys Gly Phe Tyr

743

1	5	10	15
Ile Ser Lys Ser Leu Gly Ile Leu Gly Ile Leu Leu Gly Val Ala Ala	20	25	30
Val Cys Thr Ile Ile Ala Leu Ser Val Val Tyr Ser Gln Glu Lys Asn	35	40	45
Lys Asn Ala Asn Ser Ser Pro Val Ala Ser Thr Thr Pro Ser Ala Ser	50	55	60
Ala Thr Thr Asn Pro Ala Ser Xaa Thr Thr Leu Asp Gln Ser Lys Ala	65	70	75
Trp Asn Arg Tyr Arg Leu Pro Asn Thr Leu Lys Pro Asp Ser Tyr Arg	85	90	95
Val Thr Leu Arg Pro Tyr Leu Thr Pro Asn Asp Arg Gly Leu Tyr Val	100	105	110
Phe Lys Gly Ser Ser Thr Val Arg Phe Thr Cys Lys Glu Ala Thr Asp	115	120	125
Val Ile Ile Ile His Ser Lys Lys Leu Asn Tyr Thr Leu Ser Gln Gly	130	135	140
His Arg Val Val Leu Arg Gly Val Gly Gly Ser Gln Pro Pro Asp Ile	145	150	155
Asp Lys Thr Glu Leu Val Glu Pro Thr Glu Tyr Leu Val Val His Leu	165	170	175
Lys Gly Ser Leu Val Lys Asp Ser Gln Tyr Glu Met Asp Ser Glu Phe	180	185	190
Glu Gly Glu Leu Ala Asp Asp Leu Ala Gly Phe Tyr Arg Ser Glu Tyr	195	200	205
Met Glu Gly Asn Val Arg Lys Val Val Ala Thr Thr Gln Met Gln Ala	210	215	220
Ala Asp Ala Arg Lys Ser Phe Pro Cys Phe Asp Glu Pro Ala Met Lys	225	230	235
Ala Glu Phe Asn Ile Thr Leu Ile His Pro Lys Asp Leu Thr Ala Leu	245	250	255
Ser Asn Met Leu Pro Lys Gly Pro Ser Thr Pro Leu Pro Glu Asp Pro	260	265	270
Asn Trp Asn Val Thr Glu Phe His Thr Thr Pro Lys Met Ser Thr Tyr			

744

275	280	285
Leu Leu Ala Phe Ile Val Ser Glu Phe Asp Tyr Val Glu Lys Gln Ala		
290	295	300
Ser Asn Gly Val Leu Ile Arg Ile Trp Ala Arg Pro Ser Ala Ile Ala		
305	310	315 320
Ala Gly His Gly Asp Tyr Ala Leu Asn Val Thr Gly Pro Ile Leu Asn		
325	330	335
Phe Phe Ala Gly His Tyr Asp Thr Pro Tyr Pro Leu Pro Lys Ser Asp		
340	345	350
Gln Ile Gly Leu Pro Asp Phe Asn Ala Gly Ala Met Glu Asn Trp Gly		
355	360	365
Leu Val Thr Tyr Arg Glu Asn Ser Leu Leu Phe Asp Pro Leu Ser Ser		
370	375	380
Ser Ser Ser Asn Lys Glu Arg Val Val Thr Val Ile Ala His Glu Leu		
385	390	395 400
Ala His Gln Trp Phe Gly Asn Leu Val Thr Ile Glu Trp Trp Asn Asp		
405	410	415
Leu Trp Leu Asn Glu Gly Phe Ala Ser Tyr Val Glu Tyr Leu Gly Ala		
420	425	430
Asp Tyr Ala Glu Pro Thr Trp Asn Leu Lys Asp Leu Met Val Leu Asn		
435	440	445
Asp Val Tyr Arg Val Met Ala Val Asp Ala Leu Ala Ser Ser His Pro		
450	455	460
Leu Ser Thr Pro Ala Ser Glu Ile Asn Thr Pro Ala Gln Ile Ser Glu		
465	470	475 480
Leu Phe Asp Ala Ile Ser Tyr Ser Lys Gly Ala Ser Val Leu Arg Met		
485	490	495
Leu Ser Ser Phe Leu Ser Glu Asp Val Phe Lys Gln Gly Leu Ala Ser		
500	505	510
Tyr Leu His Thr Phe Ala Tyr Gln Asn Thr Ile Tyr Leu Asn Leu Trp		
515	520	525
Asp His Leu Gln Glu Ala Val Asn Asn Arg Ser Ile Gln Leu Pro Thr		
530	535	540
Thr Val Arg Asp Ile Met Asn Arg Trp Thr Leu Gln Met Gly Phe Pro		

745

545	550	555	560
Val Ile Thr Val Asp Thr Ser Thr Gly Thr Leu Ser Gln Glu His Phe			
565		570	575
Leu Leu Asp Pro Asp Ser Asn Val Thr Arg Pro Ser Glu Phe Asn Tyr			
580	585		590
Val Trp Ile Val Pro Ile Thr Ser Ile Arg Asp Gly Arg Gln Gln Gln			
595	600		605
Asp Tyr Trp Leu Ile Asp Val Arg Ala Gln Asn Asp Leu Phe Ser Thr			
610	615		620
Ser Gly Asn Glu Trp Val Leu Leu Asn Leu Asn Val Thr Gly Tyr Tyr			
625	630	635	640
Arg Val Asn Tyr Asp Glu Glu Asn Trp Arg Lys Ile Gln Thr Gln Leu			
645	650		655
Gln Arg Asp His Ser Ala Ile Pro Val Ile Asn Arg Ala Gln Ile Ile			
660	665		670
Asn Asp Ala Phe Asn Leu Ala Ser Ala His Lys Val Pro Val Thr Leu			
675	680		685
Ala Leu Asn Asn Thr Leu Phe Leu Ile Glu Glu Arg Gln Tyr Met Pro			
690	695		700
Trp Glu Ala Ala Leu Ser Ser Leu Ser Tyr Phe Lys Leu Met Phe Asp			
705	710	715	720
Arg Ser Glu Val Tyr Gly Pro Met Lys Asn Tyr Leu Lys Lys Gln Val			
725	730		735
Thr Pro Leu Phe Ile His Phe Arg Asn Asn Thr Asn Asn Trp Arg Glu			
740	745		750
Ile Pro Glu Asn Leu Met Asp Gln Tyr Xaa Glu Val Asn Ala Ile Ser			
755	760		765
Thr Ala Cys Ser Asn Gly Val Pro Glu Cys Glu Glu Met Val Ser Gly			
770	775		780
Leu Phe Lys Gln Trp Met Glu Asn Pro Asn Asn Asn Pro Ile His Pro			
785	790	795	800
Asn Leu Arg Ser Thr Val Tyr Cys Asn Ala Ile Ala Gln Gly Gly Glu			
805	810		815
Glu Glu Trp Asp Phe Ala Trp Glu Gln Phe Arg Asn Ala Thr Leu Val			

820	825	830
Asn Glu Ala Asp Lys Leu Arg	Ala Ala Leu Ala Cys Ser Lys Glu Leu	
835	840	845
Trp Ile Leu Asn Arg Tyr Leu Ser Tyr Thr Leu Asn Pro Asp Leu Ile		
850	855	860
Arg Lys Gln Asp Ala Thr Ser Thr Ile Ile Ser Ile Thr Asn Asn Val		
865	870	875
Ile Gly Gln Gly Leu Val Trp Asp Phe Val Gln Ser Asn Trp Lys Lys		
885	890	895
Leu Phe Asn Asp Tyr Gly Gly Gly Ser Phe Ser Phe Ser Asn Leu Ile		
900	905	910
Gln Ala Val Thr Arg Arg Phe Ser Thr Glu Tyr Glu Leu Gln Gln Leu		
915	920	925
Glu Gln Phe Lys Lys Asp Asn Glu Glu Thr Gly Phe Gly Ser Gly Thr		
930	935	940
Arg Ala Leu Glu Gln Ala Leu Glu Lys Thr Lys Ala Asn Ile Lys Trp		
945	950	955
Val Lys Glu Asn Lys Glu Val Val Leu Gln Trp Phe Thr Glu Asn Ser		
965	970	975

Lys

<210> 798

<211> 851

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (7)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (267)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 798

Pro Ala Ala Asn Ser Gln Xaa Ala Ala Arg Pro Val Ala Ser Pro Arg

747

1	5	10	15
Gly Ala Tyr Lys Ala Ser Ala Thr Pro Arg Ala Pro Ala Ala Pro Tyr	20	25	30
Leu His Arg Arg Pro His Ser Ala Ala Leu Arg Ala Ala Pro Ala Ala	35	40	45
Gly Arg Ala Pro Cys Pro Pro Ala Pro Ala Arg Asn Arg Arg Leu Arg	50	55	60
Ala Asp Pro Gly Leu Cys Val Leu Ala Arg Ser Ala Ala Leu Arg Gly	65	70	75
Arg Gly Arg Leu Ser Pro Arg Gly Pro Arg Gly Pro Asn Met Gly Gly	85	90	95
Cys Thr Val Lys Pro Gln Leu Leu Leu Leu Ala Leu Val Leu His Pro	100	105	110
Trp Asn Pro Cys Leu Gly Ala Asp Ser Glu Lys Pro Ser Ser Ile Pro	115	120	125
Thr Asp Lys Leu Leu Val Ile Thr Val Ala Thr Lys Glu Ser Asp Gly	130	135	140
Phe His Arg Phe Met Gln Ser Ala Lys Tyr Phe Asn Tyr Thr Val Lys	145	150	155
Val Leu Gly Gln Gly Glu Glu Trp Arg Gly Gly Asp Gly Ile Asn Ser	165	170	175
Ile Gly Gly Gly Gln Lys Val Arg Leu Met Lys Glu Val Met Glu His	180	185	190
Tyr Ala Asp Gln Asp Asp Leu Val Val Met Phe Thr Glu Cys Phe Asp	195	200	205
Val Ile Phe Ala Gly Gly Pro Glu Glu Val Leu Lys Lys Phe Gln Lys	210	215	220
Ala Asn His Lys Val Val Phe Ala Ala Asp Gly Ile Leu Trp Pro Asp	225	230	235
Lys Arg Leu Ala Asp Lys Tyr Pro Val Val His Ile Gly Lys Arg Tyr	245	250	255
Leu Asn Ser Gly Gly Phe Ile Gly Tyr Ala Xaa Tyr Val Asn Arg Ile	260	265	270
Val Gln Gln Trp Asn Leu Gln Asp Asn Asp Asp Asp Gln Leu Phe Tyr			

275	280	285
Thr Lys Val Tyr Ile Asp Pro Leu Lys Arg Glu Ala Ile Asn Ile Thr		
290	295	300
Leu Asp His Lys Cys Lys Ile Phe Gln Thr Leu Asn Gly Ala Val Asp		
305	310	315 320
Glu Val Val Leu Lys Phe Glu Asn Gly Lys Ala Arg Ala Lys Asn Thr		
	325	330 335
Phe Tyr Glu Thr Leu Pro Val Ala Ile Asn Gly Asn Gly Pro Thr Lys		
	340	345 350
Ile Leu Leu Asn Tyr Phe Gly Asn Tyr Val Pro Asn Ser Trp Thr Gln		
	355	360 365
Asp Asn Gly Cys Thr Leu Cys Glu Phe Asp Thr Val Asp Leu Ser Ala		
	370	375 380
Val Asp Val His Pro Asn Val Ser Ile Gly Val Phe Ile Glu Gln Pro		
	385	390 395 400
Thr Pro Phe Leu Pro Arg Phe Leu Asp Ile Leu Leu Thr Leu Asp Tyr		
	405	410 415
Pro Lys Glu Ala Leu Lys Leu Phe Ile His Asn Lys Glu Val Tyr His		
	420	425 430
Glu Lys Asp Ile Lys Val Phe Phe Asp Lys Ala Lys His Glu Ile Lys		
	435	440 445
Thr Ile Lys Ile Val Gly Pro Glu Glu Asn Leu Ser Gln Ala Glu Ala		
	450	455 460
Arg Asn Met Gly Met Asp Phe Cys Arg Gln Asp Glu Lys Cys Asp Tyr		
	465	470 475 480
Tyr Phe Ser Val Asp Ala Asp Val Val Leu Thr Asn Pro Arg Thr Leu		
	485	490 495
Lys Ile Leu Ile Glu Gln Asn Arg Lys Ile Ile Ala Pro Leu Val Thr		
	500	505 510
Arg His Gly Lys Leu Trp Ser Asn Phe Trp Gly Ala Leu Ser Pro Asp		
	515	520 525
Gly Tyr Tyr Ala Arg Ser Glu Asp Tyr Val Asp Ile Val Gln Gly Asn		
	530	535 540
Arg Val Gly Val Trp Asn Val Pro Tyr Met Ala Asn Val Tyr Leu Ile		

545	550	555	560
Lys Gly Lys Thr	Leu Arg Ser Glu Met	Asn Glu Arg Asn Tyr	Phe Val
	565	570	575
Arg Asp Lys Leu	Asp Pro Asp Met Ala	Leu Cys Arg Asn Ala	Arg Glu
	580	585	590
Met Thr Leu Gln	Arg Glu Lys Asp Ser	Pro Thr Pro Glu Thr	Phe Gln
	595	600	605
Met Leu Ser Pro	Pro Lys Gly Val Phe	Met Tyr Ile Ser	Asn Arg His
	610	615	620
Glu Phe Gly Arg	Leu Leu Ser Thr Ala	Asn Tyr Asn Thr	Ser His Tyr
	625	630	635
Asn Asn Asp Leu	Trp Gln Ile Phe Glu	Asn Pro Val Asp	Trp Lys Glu
	645	650	655
Lys Tyr Ile Asn	Arg Asp Tyr Ser Lys	Ile Phe Thr Glu	Asn Ile Val
	660	665	670
Glu Gln Pro Cys	Pro Asp Val Phe Trp	Phe Pro Ile Phe	Ser Glu Lys
	675	680	685
Ala Cys Asp Glu	Leu Val Glu Glu Met	Glu His Tyr Gly	Lys Trp Ser
	690	695	700
Gly Gly Lys His	His Asp Ser Arg Ile	Ser Gly Gly Tyr	Glu Asn Val
	705	710	715
Pro Thr Asp Asp	Ile His Met Lys Gln	Val Asp Leu Glu	Asn Val Trp
	725	730	735
Leu His Phe Ile	Arg Glu Phe Ile Ala	Pro Val Thr Leu	Lys Val Phe
	740	745	750
Ala Gly Tyr Tyr	Thr Lys Gly Phe Ala	Leu Leu Asn Phe	Val Val Lys
	755	760	765
Tyr Ser Pro Glu	Arg Gln Arg Ser Leu	Arg Pro His His	Asp Ala Ser
	770	775	780
Thr Phe Thr Ile	Asn Ile Ala Leu Asn	Asn Val Gly Glu	Asp Phe Gln
	785	790	795
Gly Gly Gly Cys	Lys Phe Leu Arg Tyr	Asn Cys Ser Ile	Glu Ser Pro
	805	810	815
Arg Lys Gly Trp	Ser Phe Met His Pro	Gly Arg Leu Thr	His Leu His

750

820 825 830
 Glu Gly Leu Pro Val Lys Asn Gly Thr Arg Tyr Ile Ala Val Ser Phe
 835 840 845

Ile Asp Pro
 850

<210> 799
 <211> 138
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (126)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 799
 Phe Ala Pro Pro Phe Gly Phe Met Glu Leu Asn Tyr Ser Leu Val Gln
 1 5 10 15

Lys Val Val Thr Arg Phe Pro Pro Val Pro Gln Gln Gln Leu Leu Leu
 20 25 30

Ala Ser Leu Pro Ala Gly Ser Leu Arg Cys Ile Thr Cys Ala Val Val
 35 40 45

Gly Asn Gly Gly Ile Leu Asn Asn Ser His Met Gly Gln Glu Ile Asp
 50 55 60

Ser His Asp Tyr Val Phe Arg Leu Ser Gly Ala Leu Ile Lys Gly Tyr
 65 70 75 80

Glu Gln Asp Val Gly Thr Arg Thr Ser Phe Tyr Gly Phe Thr Ala Phe
 85 90 95

Ser Leu Thr Gln Ser Leu Leu Ile Leu Gly Asn Arg Gly Phe Lys Asn
 100 105 110

Val Pro Leu Gly Lys Asp Val Arg Tyr Leu Asp Phe Leu Xaa Ala Pro
 115 120 125

Gly Asn Met Lys Trp Leu Glu His Cys Leu
 130 135

<210> 800

751

<211> 585

<212> PRT

<213> Homo sapiens

<400> 800

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Leu Pro Leu Cys Leu Leu Met Ala Gln Gln Arg Asn Gly Val Ile Phe
 1           5           10           15

Gln Glu Gly Gly Glu Lys His Leu Lys Leu Val Gly Lys Leu Tyr Asp
 20           25           30

Gln Cys His Asp Thr Leu Val Gln Phe Gly Gly Phe Leu Ala Ser Asn
 35           40           45

Leu Ser Thr Glu Asp Tyr Ile Lys Arg Val Pro Ser Ile Asp Val Leu
 50           55           60

Cys Asn Glu Phe His Thr Pro His Asp Ala Ala Phe Phe Leu Ser Arg
 65           70           75           80

Pro Met Tyr Ala His His Ile Ser Ser Lys Tyr Asp Glu Leu Lys Lys
           85           90           95

Ser Glu Lys Gly Ser Lys Gln Gln His Lys Val His Lys Tyr Ile Thr
 100           105           110

Ser Cys Glu Met Val Met Ala Pro Val His Glu Ala Val Val Ser Leu
 115           120           125

His Val Ser Lys Val Trp Asp Asp Ile Ser Pro Gln Phe Tyr Ala Thr
 130           135           140

Phe Trp Ser Leu Thr Met Tyr Asp Leu Ala Val Pro His Thr Ser Tyr
 145           150           155           160

Glu Arg Glu Val Asn Lys Leu Lys Val Gln Met Lys Ala Ile Asp Asp
 165           170           175

Asn Gln Glu Met Pro Pro Asn Lys Lys Lys Glu Lys Glu Arg Cys
 180           185           190

Thr Ala Leu Gln Asp Lys Leu Leu Glu Glu Glu Lys Lys Gln Met Glu
 195           200           205

His Val Gln Arg Val Leu Gln Arg Leu Lys Leu Glu Lys Asp Asn Trp
 210           215           220

Leu Leu Ala Lys Ser Thr Lys Asn Glu Thr Ile Thr Lys Phe Leu Gln
 225           230           235           240

Leu Cys Ile Phe Pro Arg Cys Ile Phe Ser Ala Ile Asp Ala Val Tyr

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752

	245		250		255
Cys Ala Arg Phe Val Glu Leu Val His Gln Gln Lys Thr Pro Asn Phe					
	260		265		270
Ser Thr Leu Leu Cys Tyr Asp Arg Val Phe Ser Asp Ile Ile Tyr Thr					
	275		280		285
Val Ala Ser Cys Thr Glu Asn Glu Ala Ser Arg Tyr Gly Arg Phe Leu					
	290		295		300
Cys Cys Met Leu Glu Thr Val Thr Arg Trp His Ser Asp Arg Ala Thr					
	305		310		315
Tyr Glu Lys Glu Cys Gly Asn Tyr Pro Gly Phe Leu Thr Ile Leu Arg					
		325		330	335
Ala Thr Gly Phe Asp Gly Gly Asn Lys Ala Asp Gln Leu Asp Tyr Glu					
	340		345		350
Asn Phe Arg His Val Val His Lys Trp His Tyr Lys Leu Thr Lys Ala					
	355		360		365
Ser Val His Cys Leu Glu Thr Gly Glu Tyr Thr His Ile Arg Asn Ile					
	370		375		380
Leu Ile Val Leu Thr Lys Ile Leu Pro Trp Tyr Pro Lys Val Leu Asn					
	385		390		395
Leu Gly Gln Ala Leu Glu Arg Arg Val His Lys Ile Cys Gln Glu Glu					
		405		410	415
Lys Glu Lys Arg Pro Asp Leu Tyr Ala Leu Ala Met Gly Tyr Ser Gly					
	420		425		430
Gln Leu Lys Ser Arg Lys Ser Tyr Met Ile Pro Glu Asn Glu Phe His					
	435		440		445
His Lys Asp Pro Pro Pro Arg Asn Ala Val Ala Ser Val Gln Asn Gly					
	450		455		460
Pro Gly Gly Gly Pro Ser Ser Ser Ser Ile Gly Ser Ala Ser Lys Ser					
	465		470		475
Asp Glu Ser Ser Thr Glu Glu Thr Asp Lys Ser Arg Glu Arg Ser Gln					
		485		490	495
Cys Gly Val Lys Ala Val Asn Lys Ala Ser Ser Thr Thr Pro Lys Gly					
	500		505		510
Asn Ser Ser Asn Gly Asn Ser Gly Ser Asn Ser Asn Lys Ala Val Lys					

515	520	525
Glu Asn Asp Lys Glu Lys Gly Lys Glu Lys Glu Lys Glu Lys Lys Glu		
530	535	540
Lys Thr Pro Ala Thr Thr Pro Glu Ala Arg Val Leu Gly Lys Asp Gly		
545	550	555
Lys Glu Lys Pro Lys Glu Glu Arg Pro Asn Lys Asp Glu Lys Ala Arg		
565	570	575
Glu Thr Lys Val Lys Asn Ala Glu Val		
580	585	

<210> 801

<211> 161

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 801

Leu Ala Xaa Leu Trp Gly Asp Gly Ser Ile Met Ala Ser Met Gln Lys
1 5 10 15

Arg Leu Gln Lys Glu Leu Leu Ala Leu Gln Asn Asp Pro Pro Pro Gly
20 25 30

Met Thr Leu Asn Glu Lys Ser Val Gln Asn Ser Ile Thr Gln Trp Ile
35 40 45

Val Asp Met Glu Gly Ala Pro Gly Thr Leu Tyr Glu Gly Glu Lys Phe
50 55 60

Gln Leu Leu Phe Lys Phe Ser Ser Arg Tyr Pro Phe Asp Ser Pro Gln
65 70 75 80

Val Met Phe Thr Gly Glu Asn Ile Pro Val His Pro His Val Tyr Ser
85 90 95

Asn Gly His Ile Cys Leu Ser Ile Leu Thr Glu Asp Trp Ser Pro Ala
100 105 110

Leu Ser Val Gln Ser Val Cys Leu S r Ile Ile Ser Met Leu Ser Ser
115 120 125

Cys Lys Glu Lys Arg Arg Pro Pro Asp Asn Ser Phe Tyr Val Arg Thr
 130 135 140

Cys Asn Lys Asn Pro Lys Lys Thr Lys Trp Trp Tyr His Asp Asp Thr
 145 150 155 160

Cys

<210> 802
 <211> 298
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (18)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (216)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 802
 Arg Lys Arg Ser Leu Pro Asn Lys Gly Arg Arg Arg Pro Arg Arg Gln
 1 5 10 15

Ser Xaa Val Gln Arg Lys Lys Arg Glu Glu Glu Glu Glu Gly Gly
 20 25 30

Glu Ser Lys Ala Asp Asp Pro Tyr Ala His Leu Ser Lys Lys Glu Lys
 35 40 45

Lys Lys Leu Lys Lys Gln Met Glu Tyr Glu Arg Gln Val Ala Ser Leu
 50 55 60

Lys Ala Ala Asn Ala Ala Glu Asn Asp Phe Ser Val Ser Gln Ala Glu
 65 70 75 80

Met Ser Ser Arg Gln Ala Met Leu Glu Asn Ala Ser Asp Ile Lys Leu
 85 90 95

Glu Lys Phe Ser Ile Ser Ala His Gly Lys Glu Leu Phe Val Asn Ala
 100 105 110

Asp Leu Tyr Ile Val Ala Gly Arg Arg Tyr Gly Leu Val Gly Pro Asn
 115 120 125

755

Gly Lys Gly Lys Thr Thr Leu Leu Lys His Ile Ala Asn Arg Ala Leu
130 135 140

Ser Ile Pro Pro Asn Ile Asp Val Leu Leu Cys Glu Gln Glu Val Val
145 150 155 160

Ala Asp Glu Thr Pro Ala Val Gln Ala Val Leu Arg Ala Asp Thr Lys
165 170 175

Arg Leu Lys Leu Leu Glu Glu Glu Arg Arg Leu Gln Gly Gln Leu Glu
180 185 190

Gln Gly Asp Asp Thr Ala Ala Glu Arg Leu Glu Lys Val Tyr Glu Glu
195 200 205

Leu Arg Ala Thr Gly Ala Ala Xaa Ala Glu Ala Lys Ala Arg Arg Ile
210 215 220

Leu Ala Gly Leu Gly Phe Asp Pro Glu Met Gln Asn Arg Pro Thr Gln
225 230 235 240

Lys Phe Ser Gly Gly Trp Arg Met Arg Val Ser Leu Ala Arg Ala Leu
245 250 255

Phe Met Glu Pro Thr Leu Leu Met Leu Asp Glu Pro Thr Asn His Leu
260 265 270

Asp Leu Asn Ala Val Ile Trp Leu Asn Lys Cys Val Thr Ala Phe Ala
275 280 285

Ser Leu Val Pro Ile Leu His Phe Leu Pro
290 295

<210> 803

<211> 281

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (225)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 803

756

Gly Ala Xaa Gln Tyr Arg Gln His Ile Gln Val Phe Ile Asp Arg Phe
 1 5 10 15
 Arg Tyr Asn Ala Asn Arg Ala Ser Gln Val Gln Ser Lys Leu Lys Met
 20 25 30
 Leu Glu Lys Leu Pro Glu Leu Lys Pro Val Asp Lys Glu Ser Glu Val
 35 40 45
 Val Met Lys Phe Pro Asp Gly Phe Glu Lys Phe Ser Pro Pro Ile Leu
 50 55 60
 Gln Leu Asp Glu Val Asp Phe Tyr Tyr Asp Pro Lys His Val Ile Phe
 65 70 75 80
 Ser Arg Leu Ser Val Ser Ala Asp Leu Glu Ser Arg Ile Cys Val Val
 85 90 95
 Gly Glu Asn Gly Ala Gly Lys Ser Thr Met Leu Lys Leu Leu Leu Gly
 100 105 110
 Asp Leu Ala Pro Val Arg Gly Ile Arg His Ala His Arg Asn Leu Lys
 115 120 125
 Ile Gly Tyr Phe Ser Gln His His Val Glu Gln Leu Asp Leu Asn Val
 130 135 140
 Ser Ala Val Glu Leu Leu Ala Arg Lys Phe Pro Gly Arg Pro Glu Glu
 145 150 155 160
 Glu Tyr Arg His Gln Leu Gly Arg Tyr Gly Ile Ser Gly Glu Leu Ala
 165 170 175
 Met Arg Pro Leu Ala Ser Leu Ser Gly Gly Gln Lys Ser Arg Val Ala
 180 185 190
 Phe Ala Gln Met Thr Met Pro Cys Pro Asn Phe Tyr Ile Leu Asp Glu
 195 200 205
 Pro Thr Asn His Leu Asp Met Glu Thr Ile Glu Ala Leu Gly Arg Ala
 210 215 220
 Xaa Asn Asn Phe Arg Gly Gly Val Ile Leu Val Ser His Asp Glu Arg
 225 230 235 240
 Phe Ile Arg Leu Val Cys Arg Glu Leu Trp Val Cys Glu Gly Gly Gly
 245 250 255
 Val Thr Arg Val Glu Gly Gly Phe Asp Gln Tyr Arg Ala Leu Leu Gln
 260 265 270

757

Glu Gln Phe Arg Arg Glu Gly Phe Leu
275 280

<210> 804
<211> 65
<212> PRT
<213> Homo sapiens

<400> 804
Asn Val Leu Arg Leu Gly His Ile Lys Pro Thr Ile Phe Glu Asp His
1 5 10 15
Val Pro Ser Ala Leu Lys Thr Val Ser His Tyr Met Asn Met Thr Ile
20 25 30
Cys Ala His Leu Lys Phe Arg Ala Arg His Cys Asp Thr Asp Ala Glu
35 40 45
Ala Ser Arg Leu Val Lys Ser Leu Asp Phe Cys Gly Ile Phe Phe Val
50 55 60

Thr
65

<210> 805
<211> 166
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (92)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (124)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (132)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (144)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (145)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (165)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 805

Gly	Thr	Gly	Cys	Ile	Arg	Arg	Gly	His	Gln	Ala	Asp	His	Cys	Pro	Ser
1				5					10					15	

Ala	Met	Ala	Leu	Trp	Met	Arg	Leu	Leu	Pro	Leu	Leu	Ala	Leu	Leu	Ala
			20					25					30		

Leu	Trp	Gly	Pro	Asp	Pro	Ala	Ala	Ala	Phe	Val	Asn	Gln	His	Leu	Cys
		35					40					45			

Gly	Ser	His	Leu	Val	Glu	Ala	Leu	Tyr	Leu	Val	Cys	Gly	Glu	Arg	Gly
	50					55					60				

Phe	Phe	Tyr	Thr	Pro	Lys	Thr	Arg	Arg	Glu	Ala	Glu	Asp	Leu	Gln	Val
65					70					75					80

Gly	Gln	Val	Xaa	Leu	Gly	Gly	Gly	Pro	Gly	Ala	Xaa	Ser	Leu	Gln	Pro
				85					90					95	

Leu	Ala	Leu	Glu	Gly	Val	Pro	Ala	Xaa	Ala	Trp	His	Cys	Gly	Thr	Met
		100						105					110		

Leu	Tyr	Gln	His	Leu	Leu	Pro	Leu	Pro	Ala	Gly	Xaa	Leu	Leu	Gln	Leu
		115					120					125			

Asp	Ala	Ala	Xaa	Arg	Gln	Pro	His	Thr	Arg	Arg	Leu	Leu	His	Arg	Xaa
	130					135					140				

Xaa	Trp	Asn	Lys	Ala	Leu	Glu	Pro	Ala	Lys	Lys	Lys	Lys	Arg	Gly	Gly
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

145 150 155 160

Arg Phe Arg Gly Xaa Lys
 165

<210> 806

<211> 528

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (483)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 806

Pro Leu Thr Ser Thr Leu Gln Glu Leu Phe Leu Asn Leu Ile Pro Ser
1 5 10 15

Gln Cys Leu Gly Gly Leu Trp Gly His Arg Asp Arg Pro Gly His Ser
20 25 30

His Leu Cys Pro Ser Val Arg Ala Thr Val Thr Gln Phe Asn Lys Val
35 40 45

Ala Gly Ala Val Val Ser Ser Val Leu Gly Ala Thr Ser Thr Gly Glu
50 55 60

Gly Pro Gly Glu Val Thr Ile Arg Pro Leu Arg Pro Pro Gln Arg Ala
65 70 75 80

Arg Leu Leu Glu Lys Trp Ile Arg Val Ala Glu Glu Cys Arg Leu Leu
85 90 95

Arg Asn Phe Ser Ser Val Tyr Ala Val Val Ser Ala Leu Gln Ser Ser
100 105 110

Pro Ile His Arg Leu Arg Ala Ala Trp Gly Glu Ala Thr Arg Asp Ser
115 120 125

Leu Arg Val Phe Ser Ser Leu Cys Gln Ile Phe Ser Glu Glu Asp Asn
130 135 140

Tyr Ser Gln Ser Arg Glu Leu Leu Val Gln Glu Val Lys Leu Gln Ser
145 150 155 160

Pro Leu Glu Pro His Ser Lys Lys Ala Pro Arg Ser Gly Ser Arg Gly
165 170 175

760

Gly Gly Val Val Pro Tyr Leu Gly Thr Phe Leu Lys Asp Leu Val Met
 180 185 190

Leu Asp Ala Ala Ser Lys Asp Glu Leu Glu Asn Gly Tyr Ile Asn Phe
 195 200 205

Asp Lys Arg Arg Lys Glu Phe Ala Val Leu Ser Glu Leu Arg Arg Leu
 210 215 220

Gln Asn Glu Cys Arg Gly Tyr Asn Leu Gln Pro Asp His Asp Ile Gln
 225 230 235 240

Arg Trp Leu Gln Gly Leu Arg Pro Leu Thr Glu Ala Gln Ser His Arg
 245 250 255

Val Ser Cys Glu Val Glu Pro Pro Gly Ser Ser Asp Pro Pro Ala Pro
 260 265 270

Arg Val Leu Arg Pro Thr Leu Val Ile Ser Gln Trp Thr Glu Val Leu
 275 280 285

Gly Ser Val Gly Val Pro Thr Pro Leu Val Ser Cys Asp Arg Pro Ser
 290 295 300

Thr Gly Gly Asp Glu Ala Pro Thr Thr Pro Ala Pro Leu Leu Thr Arg
 305 310 315 320

Leu Ala Gln His Met Lys Trp Pro Ser Val Ser Ser Leu Asp Ser Ala
 325 330 335

Leu Glu Ser Ser Pro Ser Leu His Ser Pro Ala Asp Pro Ser His Leu
 340 345 350

Ser Pro Pro Ala Ser Ser Pro Arg Pro Ser Arg Gly His Arg Arg Ser
 355 360 365

Ala Ser Cys Gly Ser Pro Leu Ser Gly Gly Ala Glu Glu Ala Ser Gly
 370 375 380

Gly Thr Gly Tyr Gly Gly Glu Gly Ser Gly Pro Gly Ala Ser Asp Cys
 385 390 395 400

Arg Ile Ile Arg Val Gln Met Glu Leu Gly Glu Asp Gly Ser Val Tyr
 405 410 415

Lys Ser Ile Leu Val Thr Ser Gln Asp Lys Ala Pro Ser Val Ile Ser
 420 425 430

Arg Val Leu Lys Lys Asn Asn Arg Asp Ser Ala Val Ala Ser Glu Tyr
 435 440 445

Glu Leu Val Gln Leu Leu Pro Gly Glu Arg Glu Leu Thr Ile Pro Ala
 450 455 460
 Ser Ala Asn Val Phe Tyr Ala Met Asp Gly Ala Ser His Asp Phe Leu
 465 470 475 480
 Leu Arg Xaa Arg Arg Arg Ser Ser Thr Ala Thr Pro Gly Val Thr Ser
 485 490 495
 Gly Pro Ser Ala Ser Gly Thr Pro Pro Ser Glu Gly Gly Gly Gly Ser
 500 505 510
 Phe Pro Arg Ile Lys Ala Thr Gly Arg Lys Ile Ala Arg Ala Leu Phe
 515 520 525

<210> 807
 <211> 319
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (306)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (316)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (319)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 807
 Ala Ser Pro Gly Arg Ala Ala Gly Arg Gly Leu Ser Ala Gly Cys Thr
 1 5 10 15
 Thr Cys Arg Gly Ala Arg Pro Leu Val Lys Glu Lys Met Leu Ser Arg
 20 25 30
 Leu Arg Val Val Ser Thr Thr Cys Thr Leu Ala Cys Arg His Leu His
 35 40 45
 Ile Lys Glu Lys Gly Lys Pro Leu Met Leu Asn Pro Arg Thr Asn Lys

50	55	60
Gly Met Ala Phe Thr Leu Gln Glu Arg Gln Met Leu Gly Leu Gln Gly		
65	70	75 80
Leu Leu Pro Pro Lys Ile Glu Thr Gln Asp Ile Gln Ala Leu Arg Phe		
	85	90 95
His Arg Asn Leu Lys Lys Met Thr Ser Pro Leu Glu Lys Tyr Ile Tyr		
	100	105 110
Ile Met Gly Ile Gln Glu Arg Asn Glu Lys Leu Phe Tyr Arg Ile Leu		
	115	120 125
Gln Asp Asp Ile Glu Ser Leu Met Pro Ile Val Tyr Thr Pro Thr Val		
	130	135 140
Gly Leu Ala Cys Ser Gln Tyr Gly His Ile Phe Arg Arg Pro Lys Gly		
	145	150 155 160
Leu Phe Ile Ser Ile Ser Asp Arg Gly His Val Arg Ser Ile Val Asp		
	165	170 175
Asn Trp Pro Glu Asn His Val Lys Ala Val Val Val Thr Asp Gly Glu		
	180	185 190
Arg Ile Leu Gly Leu Gly Asp Leu Gly Val Tyr Gly Met Gly Ile Pro		
	195	200 205
Val Gly Lys Leu Cys Leu Tyr Thr Ala Cys Ala Gly Ile Arg Pro Asp		
	210	215 220
Arg Cys Leu Pro Val Cys Ile Asp Val Gly Thr Asp Asn Ile Ala Leu		
	225	230 235 240
Leu Lys Asp Pro Phe Tyr Met Gly Leu Tyr Gln Lys Arg Asp Arg Thr		
	245	250 255
Gln Gln Tyr Asp Asp Leu Ile Asp Glu Phe Met Lys Ala Ile Thr Asp		
	260	265 270
Arg Tyr Gly Arg Asn Thr Leu Ile Gln Phe Glu Asp Phe Gly Asn His		
	275	280 285
Asn Gly Ile Gln Val Leu Glu Glu Ser Thr Glu Glu Lys Tyr Cys Tyr		
	290	295 300
Phe Xaa Met Met Asp Ile Ser Arg Gly Gln Leu Xaa Val Ser Xaa		
	305	310 315

<210> 808
 <211> 434
 <212> PRT
 <213> Homo sapiens

<400> 808

Ile Arg His Glu Glu Asp Thr Val Gln Val Ser Thr Leu Leu Arg Pro
 1 5 10 15

Pro His Cys Pro Arg Met Val Gln Asp Gly Asp Phe Val Arg Tyr His
 20 25 30

Tyr Asn Gly Thr Leu Leu Asp Gly Thr Ser Phe Asp Thr Ser Tyr Ser
 35 40 45

Lys Gly Gly Thr Tyr Asp Thr Tyr Val Gly Ser Gly Trp Leu Ile Lys
 50 55 60

Gly Met Asp Gln Gly Leu Leu Gly Met Cys Pro Gly Glu Arg Arg Lys
 65 70 75 80

Ile Ile Ile Pro Pro Phe Leu Ala Tyr Gly Glu Lys Gly Tyr Gly Thr
 85 90 95

Val Ile Pro Pro Gln Ala Ser Leu Val Phe His Val Leu Leu Ile Asp
 100 105 110

Val His Asn Pro Lys Asp Ala Val Gln Leu Glu Thr Leu Glu Leu Pro
 115 120 125

Pro Gly Cys Val Arg Arg Ala Gly Ala Gly Asp Phe Met Arg Tyr His
 130 135 140

Tyr Asn Gly Ser Leu Met Asp Gly Thr Leu Phe Asp Ser Ser Tyr Ser
 145 150 155 160

Arg Asn His Thr Tyr Asn Thr Tyr Ile Gly Gln Gly Tyr Ile Ile Pro
 165 170 175

Gly Met Asp Gln Gly Leu Gln Gly Ala Cys Met Gly Glu Arg Arg Arg
 180 185 190

Ile Thr Ile Pro Pro His Leu Ala Tyr Gly Glu Asn Gly Thr Gly Asp
 195 200 205

Lys Ile Pro Gly Ser Ala Val Leu Ile Phe Asn Val His Val Ile Asp
 210 215 220

Phe His Asn Pro Ala Asp Val Val Glu Ile Arg Thr Leu Ser Arg Pro
 225 230 235 240

764

Ser Glu Thr Cys Asn Glu Thr Thr Lys Leu Gly Asp Phe Val Arg Tyr
 245 250 255
 His Tyr Asn Cys Ser Leu Leu Asp Gly Thr Gln Leu Phe Thr Ser His
 260 265 270
 Asp Tyr Gly Ala Pro Gln Glu Ala Thr Leu Gly Ala Asn Lys Val Ile
 275 280 285
 Glu Gly Leu Asp Thr Gly Leu Gln Gly Met Cys Val Gly Glu Arg Arg
 290 295 300
 Gln Leu Ile Val Pro Pro His Leu Ala His Gly Glu Ser Gly Ala Arg
 305 310 315 320
 Gly Val Pro Gly Ser Ala Val Leu Leu Phe Glu Val Glu Leu Val Ser
 325 330 335
 Arg Glu Asp Gly Leu Pro Thr Gly Tyr Leu Phe Val Trp His Lys Asp
 340 345 350
 Pro Pro Ala Asn Leu Phe Glu Asp Met Asp Leu Asn Lys Asp Gly Glu
 355 360 365
 Val Pro Pro Glu Glu Phe Ser Thr Phe Ile Lys Ala Gln Val Ser Glu
 370 375 380
 Gly Lys Gly Arg Leu Met Pro Gly Gln Asp Pro Glu Lys Thr Ile Gly
 385 390 395 400
 Asp Met Phe Gln Asn Gln Asp Arg Asn Gln Asp Gly Lys Ile Thr Val
 405 410 415
 Asp Glu Leu Lys Leu Lys Ser Asp Glu Asp Glu Glu Arg Val His Glu
 420 425 430
 Glu Leu

<210> 809
 <211> 125
 <212> PRT
 <213> Homo sapiens

<400> 809
 Gln Gly Gln Asp Lys Pro Ser Gly Leu Trp Pro Pro Gly Pro Trp Phe
 1 5 10 15

765

Pro Cys Pro Thr Thr Trp Ser Pro His Gly Trp Leu Ala Gly Cys Pro
 20 25 30
 Cys Val Cys Val Thr His Gly Val Ser Ala Gly Leu Cys Pro Gly Trp
 35 40 45
 Glu Gly Val Tyr Val Ala Leu Thr Val Leu Ala Gln Ser Trp Trp Ile
 50 55 60
 Leu Ser Met Asp Asn Asp Thr Leu Arg Ile Val Leu Val Cys Phe Ser
 65 70 75 80
 Tyr Leu Trp Gly Ile Phe Pro Leu Arg Leu Leu Gly Leu Leu Leu Pro
 85 90 95
 Gln Gly Val Leu Thr Leu Arg Leu Met Arg Gly Pro Leu Pro Val Ser
 100 105 110
 Pro Ile Leu Ser Ser Arg Glu Val Leu Thr Pro Asp Ser
 115 120 125

<210> 810

<211> 240

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (9)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (77)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (195)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 810

Asp Pro Glu Arg Trp Lys His Leu Xaa Lys Val Thr Pro Pro Gly Ser
 1 5 10 15

Ser Val Ser Thr Thr Pro Val Gln Val Val Arg Leu Gln Ser Pro Gln
 20 25 30

Ser Gln Gly Ser Met Met Pro Ser Cys Asn Arg Ser Cys Ser Cys Ser

35	40	45
Arg Gly Pro Ser Val Glu Asp Gly Lys Trp Tyr Gly Val Arg Ser Tyr		
50	55	60
Leu His Leu Phe Tyr Glu Asp Cys Ala Gly Thr Ala Xaa Ser Asp Asp		
65	70	75 80
Pro Glu Gly Pro Pro Val Leu Cys Pro Arg Arg Pro Trp Pro Ser Leu		
85	90	95
Cys Trp Lys Ile Ser Leu Ser Ser Gly Thr Leu Leu Leu Leu Leu Gly		
100	105	110
Val Ala Ala Leu Thr Thr Gly Tyr Ala Val Pro Pro Lys Leu Glu Gly		
115	120	125
Ile Gly Glu Gly Glu Phe Leu Val Leu Asp Gln Arg Ala Ala Asp Tyr		
130	135	140
Asn Gln Ala Leu Gly Thr Cys Arg Leu Ala Gly Thr Ala Leu Cys Val		
145	150	155 160
Ala Ala Gly Val Leu Leu Ala Ile Cys Leu Phe Trp Ala Met Ile Gly		
165	170	175
Trp Leu Ser Gln Asp Thr Lys Ala Glu Pro Leu Asp Pro Glu Ala Asp		
180	185	190
Ser His Xaa Glu Val Phe Gly Asp Glu Pro Glu Gln Gln Leu Ser Pro		
195	200	205
Ile Phe Arg Asn Ala Ser Gly Gln Ser Trp Phe Ser Pro Pro Ala Ser		
210	215	220
Pro Phe Gly Gln Ser Ser Val Gln Thr Ile Gln Pro Lys Arg Asp Ser		
225	230	235 240

<210> 811

<211> 855

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (479)

<220>

<221> SITE

<222> (829)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 811

Thr Asp Arg Lys His Arg Lys Ala Phe Leu Glu Ala Arg Gln Ser Leu
1 5 10 15

Glu Val Lys Met Asn Leu Glu Glu Gln Ser Gln Gln Gln Glu Asn Leu
20 25 30

Met Leu Ser Ile Leu Pro Lys His Val Ala Asp Glu Met Leu Lys Asp
35 40 45

Met Lys Lys Asp Glu Ser Gln Lys Asp Gln Gln Gln Phe Asn Thr Met
50 55 60

Tyr Met Tyr Arg His Glu Asn Val Ser Ile Leu Phe Ala Asp Ile Val
65 70 75 80

Gly Phe Thr Gln Leu Ser Ser Ala Cys Ser Ala Gln Glu Leu Val Lys
85 90 95

Leu Leu Asn Glu Leu Phe Ala Arg Phe Asp Lys Leu Ala Ala Lys Tyr
100 105 110

His Gln Leu Arg Ile Lys Ile Leu Gly Asp Cys Tyr Tyr Cys Ile Cys
115 120 125

Gly Leu Pro Asp Tyr Arg Glu Asp His Ala Val Cys Ser Ile Leu Met
130 135 140

Gly Leu Ala Met Val Glu Ala Ile Ser Tyr Val Arg Glu Lys Thr Lys
145 150 155 160

Thr Gly Val Asp Met Arg Val Gly Val His Thr Gly Thr Val Leu Gly
165 170 175

Gly Val Leu Gly Gln Lys Arg Trp Gln Tyr Asp Val Trp Ser Thr Asp
180 185 190

Val	Thr	Val	Ala	Asn	Lys	Met	Glu	Ala	Gly	Gly	Ile	Pro	Gly	Arg	Val
		195					200					205			

His Ile Ser Gln Ser Thr Met Asp Cys Leu Lys Gly Glu Phe Asp Val
210 215 220

Glu Pro Gly Asp Gly Gly Ser Arg Cys Asp Tyr Leu Glu Glu Lys Gly

225	230	235	240
Ile Glu Thr Tyr	Leu Ile Ile Ala Ser Lys	Pro Glu Val Lys Lys Thr	
	245	250	255
Ala Thr Gln Asn Gly	Leu Asn Gly Ser Ala Leu Pro Asn Gly	Ala Pro	
	260	265	270
Ala Ser Ser Lys Ser Ser Ser	Pro Ala Leu Ile Glu Thr Lys Glu Pro		
	275	280	285
Asn Gly Ser Ala His Ser Ser Gly	Ser Thr Ser Glu Lys Pro Glu Glu		
	290	295	300
Gln Asp Ala Gln Ala Asp Asn Pro Ser Phe	Pro Asn Pro Arg Arg Arg		
305	310	315	320
Leu Arg Leu Gln Asp Leu Ala Asp Arg Val Val Asp Ala Ser Glu Asp			
	325	330	335
Glu His Glu Leu Asn Gln Leu Leu Asn Glu Ala Leu Leu Glu Arg Glu			
	340	345	350
Ser Ala Gln Val Val Lys Lys Arg Asn Thr Phe Leu Leu Ser Met Arg			
	355	360	365
Phe Met Asp Pro Glu Met Glu Thr Arg Tyr Ser Val Glu Lys Glu Lys			
	370	375	380
Gln Ser Gly Ala Ala Phe Ser Cys Ser Cys Val Val Leu Leu Cys Thr			
385	390	395	400
Ala Leu Val Glu Ile Leu Ile Asp Pro Trp Leu Met Thr Asn Tyr Val			
	405	410	415
Thr Phe Met Val Gly Glu Ile Leu Leu Leu Ile Leu Thr Ile Cys Ser			
	420	425	430
Leu Ala Ala Ile Phe Pro Arg Ala Phe Pro Lys Lys Leu Val Ala Phe			
	435	440	445
Ser Thr Trp Ile Asp Arg Thr Arg Trp Ala Arg Asn Thr Trp Ala Met			
	450	455	460
Leu Ala Ile Phe Ile Leu Val Met Ala Asn Val Val Asp Met Xaa Ser			
465	470	475	480
Cys Leu Gln Tyr Tyr Thr Gly Pro Ser Asn Ala Thr Ala Gly Met Glu			
	485	490	495
Thr Glu Gly Ser Cys Leu Glu Asn Pro Lys Tyr Tyr Asn Tyr Val Ala			

500	505	510
Val Leu Ser Leu Ile Ala Thr Ile Met Leu Val Gln Val Ser His Met		
515	520	525
Val Lys Leu Thr Leu Met Leu Leu Val Ala Gly Ala Val Ala Thr Ile		
530	535	540
Asn Leu Tyr Ala Trp Arg Pro Val Phe Asp Glu Tyr Asp His Lys Arg		
545	550	555
Phe Arg Glu His Asp Leu Pro Met Val Ala Leu Glu Gln Met Gln Gly		
565	570	575
Phe Asn Pro Gly Leu Asn Gly Thr Asp Arg Leu Pro Leu Val Pro Ser		
580	585	590
Lys Tyr Ser Met Thr Val Met Val Phe Leu Met Met Leu Ser Phe Tyr		
595	600	605
Tyr Phe Ser Arg His Val Glu Lys Leu Ala Arg Thr Leu Phe Leu Trp		
610	615	620
Lys Ile Glu Val His Asp Gln Lys Glu Arg Val Tyr Glu Met Arg Arg		
625	630	635
Trp Asn Glu Ala Leu Val Thr Asn Met Leu Pro Glu His Val Ala Arg		
645	650	655
His Phe Leu Gly Ser Lys Lys Arg Asp Glu Glu Leu Tyr Ser Gln Thr		
660	665	670
Tyr Asp Glu Ile Gly Val Met Phe Ala Ser Leu Pro Asn Phe Ala Asp		
675	680	685
Phe Tyr Thr Glu Glu Ser Ile Asn Asn Gly Gly Ile Glu Cys Leu Arg		
690	695	700
Phe Leu Asn Glu Ile Ile Ser Asp Phe Asp Ser Leu Leu Asp Asn Pro		
705	710	715
Lys Phe Arg Val Ile Thr Lys Ile Lys Thr Ile Gly Ser Thr Tyr Met		
725	730	735
Ala Ala Ser Gly Val Thr Pro Asp Val Asn Thr Asn Gly Phe Ala Ser		
740	745	750
Ser Asn Lys Glu Asp Lys Ser Glu Arg Glu Arg Trp Gln His Leu Ala		
755	760	765
Asp Leu Ala Asp Phe Ala Leu Ala Met Lys Asp Thr Leu Thr Asn Ile		

770

770	775	780
Asn Asn Gln Ser Phe Asn Asn Phe Met Leu Arg Ile Gly Met Asn Lys		
785	790	795 800
Gly Gly Val Leu Ala Gly Val Ile Gly Ala Arg Lys Pro His Tyr Asp		
805	810	815
Ile Trp Gly Asn Thr Val Asn Val Ala Ser Arg Met Xaa Val His Gly		
820	825	830
Gly His Gly Gln His Ser Gly Gly Glu Gly Asn Pro Ser Ser Ser Ser		
835	840	845
Glu Glu Leu Arg Val Ser Val		
850	855	

<210> 812

<211> 207

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (9)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 812

Arg Gln Lys Gly Ala Phe Leu Arg Xaa Ser Arg Arg Ala Ala Gly Leu
1 5 10 15

Leu Leu Leu Pro Pro Arg Ala Pro Ala Ala Met Phe Asn Arg Ala Val
20 25 30

Ser Arg Leu Ser Arg Lys Arg Pro Pro Ser Asp Ile His Asp Ser Asp
35 40 45

Gly Ser Ser Ser Ser Ser His Gln Ser Leu Lys Ser Thr Ala Lys Trp
50 55 60

Ala Ala Ser Leu Glu Asn Leu Leu Glu Asp Pro Glu Gly Val Lys Arg
65 70 75 80

Phe Arg Glu Phe Leu Lys Lys Glu Phe Ser Glu Glu Asn Val Leu Phe
85 90 95

Trp Leu Ala Cys Glu Asp Phe Lys Lys Met Gln Asp Lys Thr Gln Met
100 105 110

771

Gln Glu Lys Ala Lys Glu Ile Tyr Met Thr Phe Leu Ser Ser Lys Ala
 115 120 125
 Ser Ser Gln Val Asn Val Glu Gly Gln Ser Arg Leu Asn Glu Lys Ile
 130 135 140
 Leu Glu Glu Pro His Pro Leu Met Phe Gln Lys Leu Gln Asp Gln Ile
 145 150 155 160
 Phe Asn Leu Met Lys Tyr Asp Ser Tyr Ser Arg Phe Leu Lys Ser Asp
 165 170 175
 Leu Phe Leu Lys His Lys Arg Thr Glu Glu Glu Glu Glu Asp Leu Pro
 180 185 190
 Asp Ala Gln Thr Ala Ala Lys Arg Ala Ser Arg Ile Tyr Asn Thr
 195 200 205

<210> 813
 <211> 233
 <212> PRT
 <213> Homo sapiens

<400> 813
 Ala Arg Ser Arg Ala Gly Gly Gly Gly Trp Gly Arg Ile Ala Gly Glu
 1 5 10 15
 Ile Thr Arg Arg Gly Ser Arg Ala Arg Pro Arg Pro Gly Pro Gln Cys
 20 25 30
 Pro Pro Gly Arg Pro Gly Thr Ala Met Ile Lys Ala Ile Leu Ile Phe
 35 40 45
 Asn Asn His Gly Lys Pro Arg Leu Ser Lys Phe Tyr Gln Pro Tyr Ser
 50 55 60
 Glu Asp Thr Gln Gln Gln Ile Ile Arg Glu Thr Phe His Leu Val Ser
 65 70 75 80
 Lys Arg Asp Glu Asn Val Cys Asn Phe Leu Glu Gly Gly Leu Leu Ile
 85 90 95
 Gly Gly Ser Asp Asn Lys Leu Ile Tyr Arg His Tyr Ala Thr Leu Tyr
 100 105 110
 Phe Val Phe Cys Val Asp Ser Ser Glu Ser Glu Leu Gly Ile Leu Asp
 115 120 125
 Leu Ile Gln Val Phe Val Glu Thr Leu Asp Lys Cys Phe Glu Asn Val

772

130 135 140
 Cys Glu Leu Asp Leu Ile Phe His Val Asp Lys Val His Asn Ile Leu
 145 150 155 160
 Ala Glu Met Val Met Gly Gly Met Val Leu Glu Thr Asn Met Asn Glu
 165 170 175
 Ile Val Thr Gln Ile Asp Ala Gln Asn Lys Leu Glu Lys Ser Glu Ala
 180 185 190
 Gly Leu Ala Gly Ala Pro Ala Arg Ala Val Ser Ala Val Lys Asn Met
 195 200 205
 Asn Leu Pro Glu Ile Pro Arg Asn Ile Asn Ile Gly Asp Ile Ser Ile
 210 215 220
 Lys Val Pro Asn Leu Pro Ser Phe Lys
 225 230

<210> 814
 <211> 353
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (7)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 814
 Asn Leu Ile Leu Trp Arg Xaa Ala Met Gln Leu Glu Ile Gln Val Ala
 1 5 10 15
 Leu Asn Phe Ile Ile Ser Tyr Leu Tyr Asn Lys Leu Pro Arg Arg Arg
 20 25 30
 Val Asn Ile Phe Gly Glu Glu Leu Glu Arg Leu Leu Lys Lys Lys Tyr
 35 40 45
 Glu Gly His Trp Tyr Pro Glu Lys Pro Tyr Lys Gly Ser Gly Phe Arg
 50 55 60
 Cys Ile His Ile Gly Glu Lys Val Asp Pro Val Ile Glu Gln Ala Ser
 65 70 75 80
 Lys Glu Ser Gly Leu Asp Ile Asp Asp Val Arg Gly Asn Leu Pro Gln
 85 90 95

773

Asp Leu Ser Val Trp Ile Asp Pro Phe Glu Val Ser Tyr Gln Ile Gly
 100 105 110
 Glu Lys Gly Pro Val Lys Val Leu Tyr Val Asp Asp Asn Asn Glu Asn
 115 120 125
 Gly Cys Glu Leu Asp Lys Glu Ile Lys Asn Ser Phe Asn Pro Glu Ala
 130 135 140
 Gln Val Phe Met Pro Ile Ser Asp Pro Ala Ser Ser Val Ser Ser Ser
 145 150 155 160
 Pro Ser Pro Pro Phe Gly His Ser Ala Ala Val Ser Pro Thr Phe Met
 165 170 175
 Pro Arg Ser Thr Gln Pro Leu Thr Phe Thr Thr Ala Thr Phe Ala Ala
 180 185 190
 Thr Lys Phe Gly Ser Thr Lys Met Lys Asn Ser Gly Arg Ser Asn Lys
 195 200 205
 Val Ala Arg Thr Ser Pro Ile Asn Leu Gly Leu Asn Val Asn Asp Leu
 210 215 220
 Leu Lys Gln Lys Ala Ile Ser Ser Ser Met His Ser Leu Tyr Gly Leu
 225 230 235 240
 Gly Leu Gly Ser Gln Gln Gln Pro Gln Gln Gln Gln Pro Ala Gln
 245 250 255
 Pro Pro Pro Pro Pro Pro Pro Pro Gln Gln Gln Gln Gln Lys Thr
 260 265 270
 Ser Ala Leu Ser Pro Asn Ala Lys Glu Phe Ile Phe Pro Asn Met Gln
 275 280 285
 Gly Gln Gly Ser Ser Thr Asn Gly Met Phe Pro Gly Asp Ser Pro Leu
 290 295 300
 Asn Leu Ser Pro Leu Gln Tyr Ser Asn Ala Phe Asp Val Phe Ala Ala
 305 310 315 320
 Tyr Gly Gly Leu Asn Glu Lys Ser Phe Val Asp Gly Leu Asn Phe Ser
 325 330 335
 Leu Asn Asn Met Gln Tyr Ser Asn Gln Gln Phe Gln Pro Val Met Ala
 340 345 350
 Asn

774

<210> 815
<211> 82
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (29)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 815
Leu Ser Ala Cys Phe Ala Tyr His Arg Asp Ile Ser Met Ala Val Pro
1 5 10 15
Pro Cys Arg Val Ala Tyr Gln Thr Asp Val Asp Cys Xaa Ile Ser Trp
20 25 30
Gln His Gln Ser Met Gly Cys Leu Thr Phe Trp Tyr Leu Ser Ser Asp
35 40 45
His Pro Tyr Pro Met Phe Ser Phe Lys His Tyr Pro Ala Ser Leu Phe
50 55 60
Ile Ile Arg Asn Ser Gly Pro Ser Val Trp Trp His Leu Glu Ser Phe
65 70 75 80
Val Pro

<210> 816
<211> 328
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (170)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (172)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (174)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (178)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (183)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (269)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (286)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 816

Phe	Thr	Val	Ser	Ser	Gly	Pro	Phe	Asn	Ile	Ile	Asn	Val	Ser	Leu	Ser
1				5					10					15	

Gly	Gly	Thr	Asn	Glu	Glu	Ile	Leu	Glu	Ser	Ile	Arg	Ala	Lys	Lys	Gly
			20					25					30		

Asp	Ile	Asp	Asn	Val	Lys	Ser	Pro	Thr	Gly	Glu	Glu	Thr	Glu	Lys	Asp
			35					40					45		

Lys	Asn	Glu	Thr	Glu	Asn	Asp	Ser	Lys	Asp	Ala	Glu	Lys	Asn	Arg	Glu
	50					55					60				

Glu	Phe	Glu	Asp	Gln	Ser	Leu	Glu	Lys	Asp	Ser	Asp	Asp	Lys	Thr	Pro
65					70				75						80

Asp	Asp	Asp	Pro	Glu	Gln	Gly	Lys	Ser	Glu	Val	Gly	Asp	Phe	Lys	Ser
				85					90					95	

Glu	Lys	Ser	Asn	Gly	Glu	Leu	Ser	Glu	Ser	Pro	Gly	Ala	Gly	Lys	Gly
			100					105					110		

Ala	Ser	Gly	Ser	Thr	Arg	Ile	Ile	Thr	Arg	Leu	Arg	Asn	Pro	Asp	Ser
		115					120						125		

Lys	Leu	Ser	Gln	Leu	Lys	Ser	Gln	Gln	Val	Ala	Ala	Ala	Ala	His	Glu
	130					135						140			

Ala	Asn	Lys	Leu	Phe	Lys	Glu	Gly	Lys	Glu	Val	Leu	Val	Val	Asn	Ser
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

145		150		155		160
Gln Gly Glu Ile Ser Arg Leu Ser Thr Xaa Lys Xaa Val Xaa Met Lys						
	165		170		175	
Gly Xaa Ile Asn Asn Tyr Xaa Lys Leu Gly Gln Glu Gly Lys Tyr Arg						
	180		185		190	
Val Tyr His Asn Gln Tyr Ser Thr Asn Ser Phe Ala Leu Asn Lys His						
	195		200		205	
Gln His Arg Glu Asp His Asp Lys Arg Arg His Leu Ala His Lys Phe						
	210		215		220	
Cys Leu Thr Pro Ala Gly Glu Phe Lys Trp Asn Gly Ser Val His Gly						
	225		230		235	240
Ser Lys Val Leu Thr Ile Ser Thr Leu Arg Leu Thr Ile Thr Gln Leu						
	245		250		255	
Glu Asn Asn Ile Pro Ser Ser Phe Leu His Pro Asn Xaa Ala Ser His						
	260		265		270	
Arg Ala Asn Trp Ile Lys Ala Val Gln Met Cys Ser Lys Xaa Arg Glu						
	275		280		285	
Phe Ala Leu Ala Leu Ala Ile Leu Glu Cys Ala Val Lys Pro Val Val						
	290		295		300	
Met Leu Pro Ile Trp Arg Glu Ser Leu Gly His Thr Ser Phe Leu Pro						
	305		310		315	320
Leu Ser His Asn His Val His Gln						
	325					

<210> 817

<211> 290

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (210)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (213)

<223> Xaa equals any of the naturally occurring L-amino acids

777

<220>

<221> SITE

<222> (271)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (290)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 817

Glu Leu Ile Leu Glu Pro Lys Asp Leu Tyr Ile Asp Arg Pro Leu Pro
 1 5 10 15

Tyr Leu Ile Gly Ser Lys Leu Phe Met Glu Gln Glu Asp Val Gly Leu
 20 25 30

Gly Glu Leu Ser Ser Glu Glu Gly Ser Val Gly Ser Asp Arg Gly Ser
 35 40 45

Ile Val Asp Thr Glu Glu Glu Lys Glu Glu Glu Ser Asp Glu Asp
 50 55 60

Phe Ala His His Ser Asp Asn Glu Gln Asn Gln His Thr Thr Gln Met
 65 70 75 80

Ser Asp Glu Glu Glu Asp Asp Asp Gly Cys Asp Leu Phe Ala Asp Ser
 85 90 95

Glu Lys Glu Glu Glu Asp Ile Glu Asp Ile Glu Glu Asn Thr Arg Pro
 100 105 110

Lys Arg Ser Arg Pro Thr Ser Phe Ala Asp Glu Leu Ala Ala Arg Ile
 115 120 125

Lys Gly Asp Ala Met Gly Arg Val Asp Glu Glu Pro Thr Thr Leu Pro
 130 135 140

Ser Gly Glu Ala Lys Pro Arg Lys Thr Leu Lys Glu Lys Lys Glu Arg
 145 150 155 160

Arg Thr Pro Ser Asp Asp Glu Glu Asp Asn Leu Phe Ala Pro Pro Lys
 165 170 175

Leu Thr Asp Glu Asp Phe Ser Pro Phe Gly Ser Gly Gly Gly Leu Phe
 180 185 190

Ser Gly Gly Lys Gly Leu Phe Asp Asp Glu Asp Glu Glu Ser Asp Leu
 195 200 205

Phe Xaa Glu Ala Xaa Gln Asp Arg Gln Ala Gly Ala Ser Val Lys Glu
 210 215 220
 Glu Ser Ser Ser Ser Lys Pro Gly Lys Lys Ile Pro Ala Gly Ala Val
 225 230 235 240
 Ser Val Phe Leu Gly Asp Thr Asp Val Phe Gly Ala Ala Ser Val Pro
 245 250 255
 Ser Leu Lys Glu Pro Gln Lys Pro Glu Gln Pro Thr Pro Arg Xaa Ser
 260 265 270
 Pro Tyr Gly Pro Pro Pro Thr Gly Leu Phe Asp Asp Asp Asp Gly Asp
 275 280 285
 Asp Xaa
 290

<210> 818
 <211> 117
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (15)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 818
 Lys Arg Gln Leu Ala Val Gln Ser Leu Ala Phe Asn Leu Lys Xaa Lys
 1 5 10 15
 Val Phe Cys Glu Leu Phe Pro Glu Val Val Glu Val Arg Lys Thr Glu
 20 25 30
 Val Gly Phe Ala Phe Pro Cys Val Lys Thr Leu Glu Phe His Leu Phe
 35 40 45
 Pro Lys Ser Lys Ile Cys Val Leu Lys Leu Gln Thr Ser Pro Gly Asp
 50 55 60
 Gly Ser Ser Pro Pro Gly Ala Pro Arg Gln Gly Arg Gln Lys Ala Trp
 65 70 75 80
 Ala Leu Gly Gly Gly Leu Arg Thr Ala Val Leu Val Gly Arg Gly Leu
 85 90 95
 Gly Leu Ser His Arg Gly Val Glu Leu Val Val Leu Ser Ser Gln Leu
 100 105 110

Gly Gly Val Trp Gly
115

<210> 819
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (29)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (130)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 819
Pro Gly Val Cys Cys Ser Ala Gly Ala Ser Phe Arg Arg Gly Ala Asp
1 5 10 15
Phe Asp Ser Trp Gly Gln Leu Val Glu Ala Ile Asp Xaa Tyr Gln Ile
20 25 30
Leu Ala Arg His Leu Gln Lys Glu Ala Gln Ala Gln His Asn Asn Ser
35 40 45
Glu Phe Thr Glu Glu Gln Lys Lys Thr Ile Gly Lys Ile Ala Thr Cys
50 55 60
Leu Gly Ile Ala Ser Ala Ala Leu Gln Ser Thr Gln Ser Gln Glu Glu
65 70 75 80
Phe Lys Leu Glu Asp Leu Lys Lys Leu Glu Pro Ile Leu Lys Asn Ile
85 90 95
Leu Thr Tyr Asn Lys Glu Phe Pro Phe Asp Val Gln Pro Val Pro Leu
100 105 110
Arg Arg Phe Trp His Leu Val Lys Lys Arg Ile Trp Glu Phe Gly Arg
115 120 125
Arg Xaa Lys Lys Arg Val Val Leu Gly Ala Gly Ser Pro Asp Ser Phe
130 135 140
Ser Cys Leu Glu Phe Pro Gly Thr Phe Ile Tyr Pro Arg
145 150 155

780

<210> 820

<211> 77

<212> PRT

<213> Homo sapiens

<400> 820

Arg Glu Thr Ala Cys Cys Gly Arg Asp Ala Arg Gly Ala Ala Pro Ala
1 5 10 15

Ala Met Ala Val Thr Ala Leu Ala Ala Arg Thr Trp Leu Gly Val Trp
20 25 30

Gly Val Arg Thr Met Gln Ala Arg Gly Phe Gly Ser Asp Gln Ser Glu
35 40 45

Asn Val Asp Arg Gly Ala Gly Ser Ile Arg Glu Ala Gly Gly Ala Phe
50 55 60

Gly Lys Arg Glu Gln Ala Glu Glu Glu Arg Tyr Phe Arg
65 70 75

<210> 821

<211> 74

<212> PRT

<213> Homo sapiens

<400> 821

His Leu Gly Phe Ile Gly Thr Lys Asn Lys Ser Tyr Thr Ser Cys Thr
1 5 10 15

Leu Phe Phe Glu Phe Leu Leu Met Arg Asn Ile His Phe Cys Ile Asp
20 25 30

Ser Asp Phe Lys Ile Ala Leu Ser Ala Phe Lys Gly Phe Leu Thr Ser
35 40 45

Arg Ala His Gln Asn Cys Gln Val Pro Ser Gly Ser Glu Ala Val Ser
50 55 60

Leu Gly Gly Leu Trp His Gln His Phe His
65 70

<210> 822

<211> 451

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (178)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (205)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (220)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (278)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (393)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (435)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 822
Arg Pro Leu Pro Thr Ser Thr Asn Val Lys Thr Leu Thr Gly Phe Gly
1 5 10 15
Pro Gly Leu Ala Met Glu Thr Ala Leu Arg Ser Pro Asp Arg Pro Glu
20 25 30
Cys Ile Arg Leu Tyr Ala Pro Pro Phe Ile Leu Ala Pro Val Lys Asp
35 40 45
Xaa Gln Thr Glu Leu Gly Glu Thr Phe Gly Glu Ala Gly Gln Lys Tyr
50 55 60

Asn Val Leu Phe Val Gly Tyr Cys Leu Ser His Asp Gln Arg Trp Ile
 65 70 75 80
 Leu Ala Ser Cys Thr Asp Leu Tyr Gly Glu Leu Leu Glu Thr Cys Ile
 85 90 95
 Ile Asn Ile Asp Val Pro Asn Arg Ala Arg Arg Lys Lys Ser Ser Ala
 100 105 110
 Arg Lys Phe Gly Leu Gln Lys Leu Trp Glu Trp Cys Leu Gly Leu Val
 115 120 125
 Gln Met Ser Ser Leu Pro Trp Arg Val Val Ile Gly Arg Leu Gly Arg
 130 135 140
 Ile Gly His Gly Glu Leu Lys Asp Trp Ser Cys Leu Leu Ser Arg Arg
 145 150 155 160
 Asn Leu Gln Ser Leu Ser Lys Arg Leu Lys Asp Met Cys Arg Met Cys
 165 170 175
 Gly Xaa Ser Ala Ala Asp Ser Pro Ser Ile Leu Ser Ala Cys Leu Val
 180 185 190
 Ala Met Glu Pro Gln Gly Ser Phe Val Ile Met Pro Xaa Ser Val Ser
 195 200 205
 Thr Gly Ser Val Phe Gly Arg Ser Thr Thr Leu Xaa Met Gln Thr Ser
 210 215 220
 Gln Leu Asn Thr Pro Gln Asp Thr Ser Cys Thr His Ile Leu Val Phe
 225 230 235 240
 Pro Thr Ser Ala Ser Val Gln Val Ala Ser Ala Thr Tyr Thr Thr Glu
 245 250 255
 Asn Leu Asp Leu Ala Phe Asn Pro Asn Asn Asp Gly Ala Asp Gly Met
 260 265 270
 Gly Ile Phe Asp Leu Xaa Asp Thr Gly Asp Asp Leu Asp Pro Asp Ile
 275 280 285
 Ile Asn Ile Leu Pro Ala Ser Pro Thr Gly Ser Pro Val His Ser Pro
 290 295 300
 Gly Ser His Tyr Pro His Gly Gly Asp Ala Gly Lys Gly Gln Ser Thr
 305 310 315 320
 Asp Arg Leu Leu Ser Thr Glu Pro His Glu Glu Val Pro Asn Ile Leu
 325 330 335

783

Gln Gln Pro Leu Ala Leu Gly Tyr Phe Val Ser Thr Ala Lys Ala Gly
 340 345 350
 Pro Leu Pro Asp Trp Phe Trp Ser Ala Cys Pro Gln Ala Gln Tyr Gln
 355 360 365
 Cys Pro Leu Phe Leu Lys Ala Ser Leu His Leu His Val Pro Ser Val
 370 375 380
 Gln Ser Asp Glu Leu Leu His Ser Xaa His Ser His Pro Leu Asp Ser
 385 390 395 400
 Asn Gln Thr Ser Asp Val Leu Arg Phe Val Leu Glu Gln Tyr Asn Ala
 405 410 415
 Leu Ser Trp Leu Thr Cys Asp Pro Ala Thr Gln Asp Arg Arg Ser Cys
 420 425 430
 Leu Pro Xaa His Phe Val Val Leu Asn Gln Leu Tyr Asn Phe Ile Met
 435 440 445
 Asn Met Leu
 450

<210> 823

<211> 211

<212> PRT

<213> Homo sapiens

<400> 823

Ile Leu Ile Ala Thr Asp Val Ala Ser Arg Gly Leu Asp Val Glu Asp
 1 5 10 15
 Val Lys Phe Val Ile Asn Tyr Asp Tyr Pro Asn Ser Ser Glu Asp Tyr
 20 25 30
 Val His Arg Ile Gly Arg Thr Ala Arg Ser Thr Asn Lys Gly Thr Ala
 35 40 45
 Tyr Thr Phe Phe Thr Pro Gly Asn Leu Lys Gln Ala Arg Glu Leu Ile
 50 55 60
 Lys Val Leu Glu Glu Ala Asn Gln Ala Ile Asn Pro Lys Leu Met Gln
 65 70 75 80
 Leu Val Asp His Arg Gly Gly Gly Gly Gly Gly Gly Arg Ser Arg
 85 90 95
 Tyr Arg Thr Thr Ser Ser Ala Asn Asn Pro Asn Leu Met Tyr Gln Asp

784

100 105 110
Glu Cys Asp Arg Ser Phe Glu Glu Ser Arg Met Val Ala Gly Glu Thr
115 120 125
Leu Gln Ala Ile Gly Ile Val Val Lys Pro Ile Glu Leu Val Met Leu
130 135 140
Met Ala Val Ala Met Glu Val Gln Ile Leu Pro Leu Glu His Lys Gln
145 150 155 160
Ala Asn Thr Pro Met Val Lys Ala Pro Met Gly Gln Leu Leu Met Ala
165 170 175
Pro Val Ala Ile Gln Leu Lys Asn Met Val Leu Ala Leu Met Glu Leu
180 185 190
Val Ala Pro Pro Gln Leu Gly Glu Val His Arg Ala Leu Ala Ser Ser
195 200 205
Leu Val Gly
210

<210> 824
<211> 22
<212> PRT
<213> Homo sapiens

<400> 824
Gly Arg Pro Thr Arg Pro Gly Val Ser Ser Cys Leu Pro Gly Trp Ser
1 5 10 15
Arg Thr Pro Gly Leu Lys
20

<210> 825
<211> 393
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (96)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 825
Thr Thr Val Thr Arg Cys Ser Pro Thr Val Ala Phe Val Glu Phe Pro

785

1	5	10	15
Ser Ser Pro Gln Leu Lys Asn Asp Val Ser Glu Glu Lys Asp Gln Lys	20	25	30
Lys Pro Glu Asn Glu Met Ser Gly Lys Val Glu Leu Val Leu Ser Gln	35	40	45
Lys Val Val Lys Pro Lys Ser Pro Glu Pro Glu Ala Thr Leu Thr Phe	50	55	60
Pro Phe Leu Asp Lys Met Pro Glu Ala Asn Gln Leu His Leu Pro Asn	65	70	75
Leu Asn Ser Gln Val Asp Ser Pro Ser Ser Glu Lys Ser Pro Val Xaa	85	90	95
Thr Pro Phe Lys Phe Trp Ala Trp Asp Pro Glu Glu Glu Arg Arg Arg	100	105	110
Gln Glu Lys Trp Gln Gln Glu Gln Glu Arg Leu Leu Gln Glu Arg Tyr	115	120	125
Gln Lys Glu Gln Asp Lys Leu Lys Glu Glu Trp Glu Lys Ala Gln Lys	130	135	140
Glu Val Glu Glu Glu Glu Arg Arg Tyr Tyr Glu Glu Glu Arg Lys Ile	145	150	155
Ile Glu Asp Thr Val Val Pro Phe Thr Val Ser Ser Ser Ser Ala Asp	165	170	175
Gln Leu Ser Thr Ser Ser Ser Met Thr Glu Gly Ser Gly Thr Met Asn	180	185	190
Lys Ile Asp Leu Gly Asn Cys Gln Asp Glu Lys Gln Asp Arg Arg Trp	195	200	205
Lys Lys Ser Phe Gln Gly Asp Asp Ser Asp Leu Leu Leu Lys Thr Arg	210	215	220
Glu Ser Asp Arg Leu Glu Glu Lys Gly Ser Leu Thr Glu Gly Ala Leu	225	230	235
Ala His Ser Gly Asn Pro Val Ser Lys Gly Val His Glu Asp His Gln	245	250	255
Leu Asp Thr Glu Ala Gly Ala Pro His Cys Gly Thr Asn Pro Gln Leu	260	265	270
Ala Gln Asp Pro Ser Gln Asn Gln Gln Thr Ser Asn Pro Thr His Ser			

786

275 280 285
 Ser Glu Asp Val Lys Pro Lys Thr Leu Pro Leu Asp Lys Ser Ile Asn
 290 295 300
 His Gln Ile Glu Ser Pro Ser Glu Arg Arg Lys Ser Ile Ser Gly Lys
 305 310 315 320
 Lys Leu Cys Ser Ser Cys Gly Leu Pro Leu Gly Lys Gly Ala Ala Met
 325 330 335
 Ile Ile Glu Thr Leu Asn Leu Tyr Phe His Ile Gln Cys Phe Arg Cys
 340 345 350
 Gly Ile Cys Lys Gly Gln Leu Gly Asp Ala Val Ser Gly Thr Asp Val
 355 360 365
 Arg Ile Arg Asn Gly Leu Leu Asn Cys Asn Asp Cys Tyr Met Arg Ser
 370 375 380
 Arg Ser Ala Gly Gln Pro Thr Thr Leu
 385 390

<210> 826

<211> 265

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 826

His Ser Pro Val Pro Gln Ser Leu Pro Ala Arg Cys Ala Ala Ala Glu
 1 5 10 15
 Ala Met Arg Leu Ile Gln Asn Met Cys Thr Ile Ala Glu Tyr Pro Ala
 20 25 30
 Pro Gly Asn Ala Ala Ala Ser Asp Cys Cys Val Gly Ala Ala Gly Arg
 35 40 45
 Arg Leu Val Lys Ile Ala Val Val Gly Ala Ser Gly Val Gly Lys Thr
 50 55 60
 Ala Leu Val Val Arg Phe Leu Xaa Lys Arg Phe Ile Gly Asp Tyr Glu
 65 70 75 80

787

Arg Asn Ala Gly Asn Leu Tyr Thr Arg Gln Val Gln Ile Glu Gly Glu
 85 90 95
 Thr Leu Ala Leu Gln Val Gln Asp Thr Pro Gly Ile Gln Val His Glu
 100 105 110
 Asn Ser Leu Ser Cys Ser Glu Gln Leu Asn Arg Cys Ile Arg Trp Ala
 115 120 125
 Asp Ala Val Val Ile Val Phe Ser Ile Thr Asp Tyr Lys Ser Tyr Glu
 130 135 140
 Leu Ile Ser Gln Leu His Gln His Val Gln Gln Leu His Leu Gly Thr
 145 150 155 160
 Arg Leu Pro Val Val Val Val Ala Asn Lys Ala Asp Leu Leu His Ile
 165 170 175
 Lys Gln Val Asp Pro Gln Leu Gly Leu Gln Leu Ala Ser Met Leu Gly
 180 185 190
 Cys Ser Phe Tyr Glu Val Ser Val Ser Glu Asn Tyr Asn Asp Val Tyr
 195 200 205
 Ser Ala Phe His Val Leu Cys Lys Glu Val Ser His Lys Gln Gln Pro
 210 215 220
 Ser Ser Thr Pro Glu Lys Arg Arg Thr Ser Leu Ile Pro Arg Pro Lys
 225 230 235 240
 Ser Pro Asn Met Gln Asp Leu Lys Arg Arg Phe Lys Gln Ala Leu Ser
 245 250 255
 Ala Lys Val Arg Thr Val Thr Ser Val
 260 265

<210> 827

<211> 555

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (479)

<223> xaa equals any of the naturally occurring L-amino acids

<400> 827

Asn Ile Tyr Phe Lys Glu Lys Arg Lys Arg Gly Gly Ala Lys Met Ala
 1 5 10 15

Gly Ala Ile Ile Glu Asn Met Ser Thr Lys Lys Leu Cys Ile Val Gly
 20 25 30

Gly Ile Leu Leu Val Phe Gln Ile Ile Ala Phe Leu Val Gly Gly Leu
 35 40 45

Ile Ala Pro Gly Pro Thr Thr Ala Val Ser Tyr Met Ser Val Lys Cys
 50 55 60

Val Asp Ala Arg Lys Asn His His Lys Thr Lys Trp Phe Val Pro Trp
 65 70 75 80

Gly Pro Asn His Cys Asp Lys Ile Arg Asp Ile Glu Glu Ala Ile Pro
 85 90 95

Arg Glu Ile Glu Ala Asn Asp Ile Val Phe Ser Val His Ile Pro Leu
 100 105 110

Pro His Met Glu Met Ser Pro Trp Phe Gln Phe Met Leu Phe Ile Leu
 115 120 125

Gln Leu Asp Ile Ala Phe Lys Leu Asn Asn Gln Ile Arg Glu Asn Ala
 130 135 140

Glu Val Ser Met Asp Val Ser Leu Ala Tyr Arg Asp Asp Ala Phe Ala
 145 150 155 160

Glu Trp Thr Glu Met Ala His Glu Arg Val Pro Arg Lys Leu Lys Cys
 165 170 175

Thr Phe Thr Ser Pro Lys Thr Pro Glu His Glu Gly Arg Tyr Tyr Glu
 180 185 190

Cys Asp Val Leu Pro Phe Met Glu Ile Gly Ser Val Ala His Lys Phe
 195 200 205

Tyr Leu Leu Asn Ile Arg Leu Pro Val Asn Glu Lys Lys Lys Ile Asn
 210 215 220

Val Gly Ile Gly Glu Ile Lys Asp Ile Arg Leu Val Gly Ile His Gln
 225 230 235 240

Asn Gly Gly Phe Thr Lys Val Trp Phe Ala Met Lys Thr Phe Leu Thr
 245 250 255

Pro Ser Ile Phe Ile Ile Met Val Trp Tyr Trp Arg Arg Ile Thr Met
 260 265 270

Met Ser Arg Pro Pro Val Leu Leu Glu Lys Val Ile Phe Ala Leu Gly
 275 280 285

Ile Ser Met Thr Phe Ile Asn Ile Pro Val Glu Trp Phe Ser Ile Gly			
290	295	300	
Phe Asp Trp Thr Trp Met Leu Leu Phe Gly Asp Ile Arg Gln Gly Ile			
305	310	315	320
Phe Tyr Ala Met Leu Leu Ser Phe Trp Ile Ile Phe Cys Gly Glu His			
	325	330	335
Met Met Asp Gln His Glu Arg Asn His Ile Ala Gly Tyr Trp Lys Gln			
	340	345	350
Val Gly Pro Ile Ala Val Gly Ser Phe Cys Leu Phe Ile Phe Asp Met			
	355	360	365
Cys Glu Arg Gly Val Gln Leu Thr Asn Pro Phe Tyr Ser Ile Trp Thr			
	370	375	380
Thr Asp Ile Gly Thr Glu Leu Ala Met Ala Phe Ile Ile Val Ala Gly			
385	390	395	400
Ile Cys Leu Cys Leu Tyr Phe Leu Phe Leu Cys Phe Met Val Phe Gln			
	405	410	415
Val Phe Arg Asn Ile Ser Gly Lys Gln Ser Ser Leu Pro Ala Met Ser			
	420	425	430
Lys Val Arg Arg Leu His Tyr Glu Gly Leu Ile Phe Arg Phe Lys Phe			
	435	440	445
Leu Met Leu Ile Thr Leu Ala Cys Ala Ala Met Thr Val Ile Phe Phe			
	450	455	460
Ile Val Ser Gln Val Thr Glu Gly His Trp Lys Trp Gly Gly Xaa Thr			
465	470	475	480
Val Gln Val Asn Ser Ala Phe Phe Thr Gly Ile Tyr Gly Met Trp Asn			
	485	490	495
Leu Tyr Val Phe Ala Leu Met Phe Leu Tyr Ala Pro Ser His Lys Asn			
	500	505	510
Tyr Gly Glu Asp Gln Ser Asn Gly Asp Leu Gly Val His Ser Gly Glu			
	515	520	525
Glu Leu Gln Leu Thr Thr Thr Ile Thr His Val Asp Gly Pro Thr Glu			
	530	535	540
Ile Tyr Lys Leu Thr Arg Lys Glu Ala Gln Glu			
	545	550	555

<210> 828

<211> 292

<212> PRT

<213> Homo sapiens

<400> 828

Leu Glu Gly Gly Thr Met Gln Glu Leu His Leu Leu Trp Trp Ala Leu
1 5 10 15

Leu Leu Gly Leu Ala Gln Ala Cys Pro Glu Pro Cys Asp Cys Gly Glu
20 25 30

Lys Tyr Gly Phe Gln Ile Ala Asp Cys Ala Tyr Arg Asp Leu Glu Ser
35 40 45

Val Pro Pro Gly Phe Pro Ala Asn Val Thr Thr Leu Ser Leu Ser Ala
50 55 60

Asn Arg Leu Pro Gly Leu Pro Glu Gly Ala Phe Arg Glu Val Pro Leu
65 70 75 80

Leu Gln Ser Leu Trp Leu Ala His Asn Glu Ile Arg Thr Val Ala Ala
85 90 95

Gly Ala Leu Ala Ser Leu Ser His Leu Lys Ser Leu Asp Leu Ser His
100 105 110

Asn Leu Ile Ser Asp Phe Ala Trp Ser Asp Leu His Asn Leu Ser Ala
115 120 125

Leu Gln Leu Leu Lys Met Asp Ser Asn Glu Leu Thr Phe Ile Pro Arg
130 135 140

Asp Ala Phe Arg Ser Leu Arg Ala Leu Arg Ser Leu Gln Leu Asn His
145 150 155 160

Asn Arg Leu His Thr Leu Ala Glu Gly Thr Phe Thr Pro Leu Thr Ala
165 170 175

Leu Ser His Leu Gln Ile Asn Glu Asn Pro Phe Asp Cys Thr Cys Gly
180 185 190

Ile Val Trp Leu Lys Thr Trp Ala Leu Thr Thr Ala Val Ser Ile Pro
195 200 205

Glu Gln Asp Asn Ile Ala Cys Thr Ser Pro His Val Leu Lys Gly Thr
210 215 220

Pro Leu Ser Arg Leu Pro Pro Leu Pro Cys Ser Ala Pro Ser Val Gln
 225 230 235 240

Leu Ser Tyr Gln Pro Ser Gln Asp Gly Ala Glu Leu Arg Pro Gly Phe
 245 250 255

Val Leu Ala Leu His Cys Asp Val Asp Gly Gln Pro Ala Pro Ala Ala
 260 265 270

Ser Leu Ala His Pro Asp Thr Gln Trp His Cys Gly Asp His Gln Pro
 275 280 285

Gln Arg Gly His
 290

<210> 829
 <211> 85
 <212> PRT
 <213> Homo sapiens

<400> 829
 Lys Thr Gly Lys Arg Trp His Leu Gln Gly Asn Thr Arg Ala Ala Gln
 1 5 10 15

Lys Ser Cys Trp Asp Glu Glu Leu Gln Thr Cys Val Val Asp Phe Leu
 20 25 30

Ala Phe Cys Leu Phe Tyr Ser Gln Gly Trp Gly Ile Thr Thr Lys Glu
 35 40 45

Val Val Phe Trp Pro Gly Val Val Ala His Ala Cys Asn Pro Ser Thr
 50 55 60

Leu Gly Gly Arg Gly Arg Val Asp His Lys Val Arg Arg Ser Arg Pro
 65 70 75 80

Ser Trp Leu Thr Arg
 85

<210> 830
 <211> 48
 <212> PRT
 <213> Homo sapiens

<400> 830
 Asp Gly Ala Cys Ser Val Ala Gln Ala Gly Val Pro Trp His Asp Leu
 1 5 10 15

Gly Ser Leu Gln Ala Pro Pro Pro Gly Phe Thr Pro Phe Ser Cys Leu
20 25 30
Ser Leu Pro Ser Ser Trp Glu Tyr Arg Arg Pro Pro Pro Arg Leu Gly
35 40 45

<210> 831
<211> 47
<212> PRT
<213> Homo sapiens

<400> 831
Ala Thr Pro Gly Leu Phe Arg Ile Phe Ser Arg Asp Gly Phe Pro His
1 5 10 15
Val Gly Gln Ala Gly Leu Glu Leu Leu Thr Ser Ser Asp Pro Pro Gly
20 25 30
Ser Ala Tyr Arg Ser Ala Glu Ile Pro Gly Val Ser His Arg Ala
35 40 45

<210> 832
<211> 28
<212> PRT
<213> Homo sapiens

<400> 832
Ser Ile Arg Leu Gly Leu Leu Lys Cys Arg Asp Tyr Arg His Tyr Pro
1 5 10 15
Leu Cys Pro Val Thr Ile Glu Ile Ile Thr Leu Gln
20 25

<210> 833
<211> 22
<212> PRT
<213> Homo sapiens

<400> 833
Phe Cys Ile Ser Arg Asp Gly Val Ser Pro Cys Trp Pro Gly Trp Ser
1 5 10 15

Gln Thr Pro Gly Leu Lys

20

<210> 834

<211> 52

<212> PRT

<213> Homo sapiens

<220>

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<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (20)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (49)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 834

Ser Gln Leu Leu Gly Xaa Leu Arg Gln Glu Asn Arg Leu Asn Pro Gly

1

5

10

15

Gly Gly Asp Xaa Ser Glu Pro Arg Ser His His Cys Thr Pro Val Trp

20

25

30

Gln Gln Arg Gln Asp Ser Ile Ser Lys Arg Lys Glu Lys Lys Thr Leu

35

40

45

Xaa Leu Tyr Ser

50

<210> 835

<211> 86

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (15)
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<222> (65)
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<222> (66)
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<222> (67)
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<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<400> 835

795

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Asn Ser Val Ser Thr Xaa Asp Thr Lys Asn Ser Gln Ala Trp Xaa Gln
 1             5             10             15

Ala Pro Val Ile Pro Ala Thr Arg Glu Ala Lys Ala Gly Glu Leu Leu
      20             25             30

Glu Leu Arg Gly Trp Arg Leu Gln Xaa Val Glu Ile Val Pro Leu His
      35             40             45

Ser Ser Leu Gly Asn Arg Ala Arg Leu Cys Leu Xaa Lys Lys Xaa Xaa
      50             55             60

Xaa Xaa Xaa Glu Lys Gln His Xaa Gly Val Ser Val Asn Leu Ser Ser
      65             70             75             80

Ala Ala Leu Leu Ile Xaa
      85

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<210> 836
 <211> 46
 <212> PRT
 <213> Homo sapiens

<220>
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 <222> (4)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (6)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (28)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (42)
 <223> Xaa equals any of the naturally occurring L-amino acids

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<400> 836
Leu Leu Glu Xaa Phe Xaa Ala His Arg Pro Gln Trp Glu Gly Val Val
 1             5             10             15

Phe Pro Arg Glu Ser Val Thr Asp His Val Asn Xaa Leu Thr Pro Leu
      20             25             30

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Val Lys Pro Val Thr Glu Leu Tyr Leu Xaa Phe Ser Ser Leu
 35 40 45

<210> 837
 <211> 129
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (77)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (125)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 837
 Ile Ala Asn Ile Arg Asn Glu Arg Val Asp Ile Thr Thr Asp Pro Met
 1 5 10 15

Asp Ile Arg Arg Ile Ile Lys Glu Cys Ser Glu Gln Leu Tyr Ala His
 20 25 30

Ile Phe Asp Asn Leu Asp Glu Met Glu Gln Val Leu Glu Arg His Asn
 35 40 45

Leu Pro Lys Leu Thr Gln Glu Glu Ile Asp His Leu Asn Arg Pro Ile
 50 55 60

Ser Ile Leu Lys Phe Glu Ser Ile Ile Asn Asn Phe Xaa Lys Gln Lys
 65 70 75 80

Ala Leu Gly Pro Asp Val Phe Ala Gly Glu Phe Tyr Gln Thr Tyr Lys
 85 90 95

Glu Asp Ile Ile Pro Ile Ile Tyr Asn Leu Phe Trp Arg Ile Glu Ala
 100 105 110

Glu Gly Asn Thr Phe Trp Leu Ile Leu Gly Gly Gln Xaa Tyr Ser Asn
 115 120 125

Thr

<210> 838
 <211> 76
 <212> PRT
 <213> Homo sapiens

<220>
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 <222> (15)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (60)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 838
 Tyr Thr Leu Leu Glu Leu Glu Leu Pro Arg Leu Leu Ala Pro Xaa Leu
 1 5 10 15
 Pro Ser Asn Gly Ser Ser Leu Lys Asp Leu Lys Trp Thr His Ser Asn
 20 25 30
 Tyr Arg Ala Ser Lys Glu Ser Cys Ile Val Ile Phe Arg His Tyr Leu
 35 40 45
 Pro Gly Ser Gly Met Gly Asn Leu Arg Xaa Cys Xaa Leu Pro Trp Met
 50 55 60
 Trp Glu Pro Phe Leu Arg Ser Leu Ser Gly Ile Gly
 65 70 75

<210> 839
 <211> 102
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (52)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (60)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (67)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (100)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 839

Thr Thr Ile Arg Ile Ser Ile Thr Ser Glu Arg Ser Thr Pro Leu Thr
1 5 10 15

Thr Leu Leu Val Ser Thr Thr Leu Pro Thr Ser Phe Pro Gly Ala Ser
20 25 30

Ile Ala Ser Thr Pro Pro Leu Asp Thr Ser Thr Thr Phe Thr Pro Ser
35 40 45

Thr Asp Thr Xaa Ser Thr Pro Thr Ile Pro Val Xaa Thr Thr Ile Ser
50 55 60

Val Ser Xaa Ile Thr Glu Gly Ser Thr Pro Gly Thr Thr Ile Phe Ile
65 70 75 80

Pro Ser Thr Pro Val Thr Ser Ser Thr Ala Asp Asp Phe Pro Ala Thr
85 90 95

Thr Gly Ala Xaa Ser Thr
100

<210> 840

<211> 81

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (75)

<223> Xaa equals any of the naturally occurring L-amino acids

799

<220>

<221> SITE

<222> (76)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (79)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 840

Pro Arg Ser Pro Ser Gly Ser Ala Met Pro Cys Ser Glu Glu Thr Pro
1 5 10 15

Ala Ile Ser Pro Ser Lys Arg Ala Arg Pro Ala Glu Val Gly Gly Met
20 25 30

Gln Leu Arg Phe Ala Arg Leu Ser Glu His Ala Thr Ala Pro Thr Arg
35 40 45

Gly Ser Ala Arg Ala Ala Gly Tyr Asp Leu Tyr Ser Ala Tyr Asp Tyr
50 55 60

Thr Ile Pro Pro Met Glu Lys Xaa Pro Pro Xaa Xaa Asn Ala Xaa Asp
65 70 75 80

Ser

<210> 841

<211> 55

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (44)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 841

Gln Ala Arg Val Gln Trp Leu Phe Thr Asp Ala Asn Ile Val His Cys
1 5 10 15

Ser Leu Gln Leu Leu Ala Ser Ser Asp Pro Pro Val Ser Thr Ser Gln
20 25 30

Val Gly Leu Gln Ala Cys Ala Asp Asp Ala Gln Xaa Pro Glu Leu Cys
35 40 45

800

Leu Ser Leu Ser Pro Thr Thr
50 55

<210> 842
<211> 99
<212> PRT
<213> Homo sapiens

<400> 842
Leu Tyr Gly Cys Glu Lys Thr Thr Glu Gly Gly Gln Pro Leu Phe Gln
1 5 10 15

Pro Leu Ala Gly Phe His His Cys Cys Ser Cys Ser Thr Ala Leu Phe
20 25 30

Arg Thr Gln Thr Thr Ala Ala Ala Val Pro Arg Met Val Ile Arg Val
35 40 45

Tyr Ile Ala Ser Ser Ser Gly Ser Thr Ala Ile Lys Lys Lys Gln Gln
50 55 60

Asp Val Leu Gly Phe Leu Glu Ala Asn Lys Ile Gly Phe Glu Glu Lys
65 70 75 80

Asp Ile Ala Ala Asn Glu Glu Asn Arg Lys Trp Met Arg Glu Asn Val
85 90 95

Pro Gly Lys

<210> 843
<211> 66
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

801

<222> (52)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 843

Ser Arg Lys Val Pro Thr Phe Xaa Thr Pro Trp Pro Asp Phe Val Pro
1 5 10 15

Arg Ala Gly Gly Glu Asn Tyr Lys Glu Phe Ser Glu Leu Leu Pro Asn
20 25 30

Arg Gln Gly Leu Lys Lys Ala Asp Xaa Ser Phe Trp Ser Lys Tyr Ile
35 40 45

Ser Ser Leu Xaa Thr Ser Ala Asp Gly Ala Lys Gly Gly Ala Val Ser
50 55 60

Arg Glu
65

<210> 844

<211> 144

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (111)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (117)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (135)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (136)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 844

Phe Val Glu Gly Val Asn Lys Lys Leu Gly Leu Leu Gly Asp Ser Leu
1 5 10 15

Asp Ile Phe Lys Gly Ile Pro Phe Ala Ala Pro Thr Lys Ala Leu Glu

802

20	25	30
Asn Pro Gln Pro His Pro Gly Trp Gln Gly Thr Leu Lys Ala Lys Asn		
35	40	45
Phe Lys Lys Arg Cys Leu Gln Ala Thr Ile Thr Gln Asp Ser Thr Tyr		
50	55	60
Gly Asp Glu Asp Cys Leu Tyr Leu Asn Ile Trp Val Pro Gln Gly Arg		
65	70	75 80
Lys Gln Val Ser Arg Asp Leu Pro Val Met Ile Trp Ile Tyr Gly Gly		
85	90	95
Ala Phe Leu Met Gly Ser Gly His Gly Ala Asn Phe Leu Asn Xaa Tyr		
100	105	110
Leu Tyr Asp Gly Xaa Glu Ile Ala Thr Arg Gly Asn Val Ile Val Val		
115	120	125
Thr Phe Asn Tyr Pro Cys Xaa Xaa Pro Trp Val Leu Thr Leu Gly Thr		
130	135	140

<210> 845

<211> 83

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (74)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (80)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (81)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 845

His Ser Val Leu Pro Pro Leu Arg Arg Arg Val Ser Leu Pro Val Ala
1 5 10 15

Met Glu Glu Glu Ile Ala Ala Leu Val Ile Asp Asn Gly Ser Gly Met
20 25 30

Cys Lys Ala Gly Phe Ala Gly Glu Arg Arg Ser Pro Ser Arg Val Ser
35 40 45

Phe His Arg Arg Ala Pro Gln Asp Thr Arg Ala Ser Trp Trp Gly Met
50 55 60

Gly Gln Lys Gly Leu Leu Leu Xaa Ala Xaa Lys Ala Gln Asn Lys Xaa
65 70 75 80

Xaa Leu Pro

<210> 846

<211> 168

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (44)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (100)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (114)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (136)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (139)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (166)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 846

Glu Lys Gln Val Arg Val Leu Thr Asp Ala Val Asp Asp Ile Thr Ser
1 5 10 15

Ile Asp Asp Phe Leu Ala Val Ser Glu Asn His Ile Leu Glu Asp Val
20 25 30

Asn Lys Cys Val Ile Ala Leu Gln Glu Lys Asp Xaa Asp Gly Leu Asp
35 40 45

Arg Thr Ala Gly Ala Ile Arg Gly Arg Ala Ala Arg Val Ile His Val
50 55 60

Val Thr Ser Glu Met Asp Asn Tyr Glu Pro Gly Val Tyr Thr Glu Lys
65 70 75 80

Val Leu Glu Ala Thr Lys Leu Leu Ser Asn Thr Val Met Pro Arg Arg
85 90 95

Ser Gln Pro Xaa Lys Pro Ser Ala Arg Thr Leu Pro Ser Pro Trp Met
100 105 110

Arg Xaa Ser Leu Ser Met Leu Pro Ala Trp Tyr Met Met Ala Ser Gly
115 120 125

Asp Ile Arg Lys Ala Val Leu Xaa Ile Arg Xaa Pro Leu Arg Ser Trp
130 135 140

Met Thr Leu Thr Leu Arg Gln Glu Asp Leu Met Ser Glu Ala Gly Arg
145 150 155 160

Ala Ser Arg Gln Lys Xaa Ile Ser
165

<210> 847

<211> 109

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (79)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (93)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 847

Gln	Asn	Ser	Gly	Cys	Leu	Thr	Met	Ala	Trp	Ile	Pro	Leu	Leu	Leu	Pro
1				5					10				15		
Leu	Leu	Thr	Leu	Cys	Thr	Gly	Ser	Glu	Ala	Ser	Tyr	Glu	Leu	Thr	Gln
			20					25					30		
Pro	Pro	Ser	Val	Ser	Val	Ser	Pro	Gly	Gln	Thr	Ala	Arg	Ile	Thr	Cys
		35					40					45			
Ser	Gly	Asp	Ala	Leu	Pro	Lys	Gln	Tyr	Ala	Tyr	Trp	Tyr	Gln	Gln	Arg
	50					55					60				
Pro	Gly	Gln	Ala	Pro	Val	Gln	Val	Ile	Tyr	Lys	Asp	Ser	Glu	Xaa	Ala
65					70					75				80	
Ser	Arg	Ile	Pro	Glu	Arg	Ile	Ser	Gly	Ser	Ser	Ser	Xaa	Thr	Thr	Val
					85				90					95	
Thr	Leu	Thr	Ile	Gln	Trp	Gly	Pro	Ser	Lys	Lys	Gln	Ser			
			100						105						

<210> 848

<211> 145

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (1)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (5)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

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<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (140)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 848

Xaa Lys Phe Ser Xaa Glu Glu Asp Gly Arg Xaa Ser Asp Xaa Glu Gly
 1 5 10 15

Ala Glu Gly His Xaa Asp Ser Gln Ser Ala Ser Gly Glu Glu Arg Pro
 20 25 30

Pro Glu Ala Asp Gly Lys Lys Gly Asn Ser Pro Asn Ser Glu Pro Pro
 35 40 45

Thr Pro Lys Xaa Ala Trp Ala Glu Thr Ser Arg Pro Pro Glu Thr Glu
 50 55 60

Pro Gly Pro Pro Ala Pro Lys Xaa Pro Leu Pro Pro Pro Xaa Arg Gly
 65 70 75 80

Pro Ala Gly Asn Trp Gly Pro Pro Gly Asp Tyr Pro Asp Arg Xaa Gly
 85 90 95

Leu Pro Ala Ser Pro Gln His Leu Glu Val Glu Asp Glu Ala Trp Arg
 100 105 110

His Asp Glu Ser Xaa Arg Leu Leu Asn Phe Leu Gly Ile Gly Arg Xaa
 115 120 125

Arg Arg Arg Xaa Glu Glu Lys Ala Ala Val Xaa Xaa Ser Ser Arg Gly
 130 135 140

Gln
 145

<210> 849

<211> 109

<212> PRT

<213> Homo sapiens

<220>

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<222> (7)

<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (27)
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<220>
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<222> (37)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (46)
<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (91)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (97)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 849
Xaa Val Arg Leu Leu Val Xaa Val Arg Asn Ser Arg Val Asp Pro Leu
1 5 10 15
Val Arg Pro Asn Met Gly Asp Ser Ala Val Xaa Thr His Trp Glu Pro
20 25 30
Tyr Thr Thr Glu Xaa Xaa Gly Tyr Leu Glu Ile Thr Lys Xaa Met Gly
35 40 45
Ser Xaa Ser Met Lys Trp Ser Leu Xaa Thr Asn Phe Leu Arg Tyr Trp
50 55 60
Thr Leu Xaa Tyr Leu Ala Leu Pro Thr Val Asn Arg Pro Xaa Xaa His
65 70 75 80
Pro Cys Ala Pro His Arg Gly Thr Pro Xaa Xaa Leu Pro Cys Ser Pro
85 90 95
Xaa Gly Glu Ser Glu Asp Cys Pro His Ala Gly His Arg
100 105

<210> 850
<211> 200
<212> PRT
<213> Homo sapiens

<220>
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<222> (140)
<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE

<222> (168)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (180)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 850

Leu Asp Ile Thr Val Met Val Phe His His Phe Gly Lys Asp Phe Pro
 1 5 10 15

Lys Ser Glu Lys Leu Ser Pro Asp Ala Phe Ile Gln Met Ala Leu Gln
 20 25 30

Leu Ala Tyr Tyr Arg Ile Tyr Gly Gln Ala Cys Ala Thr Tyr Glu Ser
 35 40 45

Ala Ser Leu Arg Met Phe His Leu Gly Arg Thr Asp Thr Ile Arg Ser
 50 55 60

Ala Ser Met Asp Ser Leu Thr Phe Val Lys Ala Met Asp Asp Ser Ser
 65 70 75 80

Val Thr Glu His Gln Lys Val Glu Leu Leu Arg Lys Ala Val Gln Ala
 85 90 95

His Arg Gly Tyr Thr Asp Arg Ala Ile Arg Gly Glu Ala Phe Asp Arg
 100 105 110

His Leu Leu Gly Leu Lys Leu Gln Ala Ile Glu Asp Leu Val Ser Met
 115 120 125

Pro Asp Ile Phe Met Asp Thr Phe Tyr Ala Ile Xaa Met His Phe Thr
 130 135 140

Ser Ser Gln Pro Gly Pro Ala Arg Gln Met Cys Met Ser Ser Gly Pro
 145 150 155 160

Trp Ser Arg Arg Leu Arg Xaa Xaa Tyr Asn Pro Trp Arg Pro His Asn
 165 170 175

Phe Ser Leu Xaa Ala Thr Gln Leu Arg Gly Asp Asn Ala Ala Ala Gly
 180 185 190

His Thr Glu Lys Ala Leu Glu Ser
 195 200

<210> 851

<211> 144

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (123)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (129)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (132)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 851

Ile	Asn	Gln	Gly	Leu	Phe	Glu	Leu	Leu	Phe	Phe	Trp	Asn	Thr	Ser	Leu
1				5					10					15	

Ser	His	Ala	Gln	Gln	Tyr	Arg	Trp	Tyr	Gln	Met	Leu	Tyr	Gln	Ala	Gly
			20					25					30		

Val	Phe	Ala	Ser	Arg	Ser	Ser	Leu	Arg	Cys	Cys	Arg	Ile	Arg	Phe	Thr
		35					40					45			

Trp	Ala	Leu	Ala	Leu	Leu	Gln	Cys	Leu	Asn	Leu	Val	Phe	Leu	Leu	Ala
	50					55					60				

Asp	Val	Trp	Phe	Gly	Phe	Leu	Pro	Ser	Ile	Tyr	Leu	Val	Phe	Leu	Ile
65					70					75					80

Ile	Leu	Tyr	Glu	Gly	Leu	Leu	Gly	Gly	Ala	Leu	Thr	Val	Asn	Thr	Phe
			85						90					95	

His	Asn	Ile	Ala	Leu	Glu	Thr	Ser	Asp	Glu	His	Arg	Glu	Phe	Ala	Met
			100					105					110		

Gly	Gly	Asn	Cys	Ile	Leu	Lys	Asn	Gly	Asp	Xaa	Leu	Ser	Gly	Ser	Gly
		115					120					125			

Xaa	Ala	Leu	Xaa	Ile	Pro	Trp	Gln	Ser	Leu	Lys	Ser	Gly	Leu	Arg	Glu
		130				135						140			

<210> 852
<211> 135
<212> PRT
<213> Homo sapiens

<220>
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<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (40)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (62)
<223> Xaa equals any of the naturally occurring L-amino acids

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<220>
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<220>
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<222> (116)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (120)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (129)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 852

Thr	Ser	Gly	Ser	Lys	Xaa	Phe	Gly	Gln	Xaa	Gly	Leu	Val	Ser	His	Xaa
1				5					10					15	

Arg	Thr	Thr	Thr	Arg	Pro	Ser	Pro	Tyr	Asp	Asp	Leu	Thr	Tyr	Gly	Glu
			20					25					30		

Gly	Glu	Glu	Asn	Pro	Asp	Gln	Xaa	Thr	Asp	Pro	Gly	Ala	Gly	Ala	Glu
		35					40					45			

Ile	Pro	Thr	Ser	Thr	Xaa	Asp	Thr	Ser	Asn	Ser	Ser	Asn	Xaa	Ala	Pro
	50					55					60				

Pro	Pro	Gly	Glu	Gly	Ala	Asp	Asp	Leu	Glu	Gly	Glu	Phe	Thr	Glu	Glu
65					70					75					80

Thr	Ile	Arg	Asn	Leu	Asp	Xaa	Asn	Tyr	Tyr	Asp	Pro	Tyr	Tyr	Asp	Pro
			85						90					95	

Thr	Ser	Ser	Pro	Val	Gly	Asp	Arg	Xaa	Gly	Asn	Ala	Gly	Glu	Pro	Gly
			100					105					110		

Tyr	His	Leu	Xaa	Arg	Asp	Leu	Xaa	Thr	Ser	Gly	Arg	Glu	Arg	Pro	Lys
		115					120					125			

Xaa	Gly	Thr	Ile	Asp	Phe	Glu
	130				135	

<210> 853

<211> 70

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (2)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (6)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (10)
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<220>
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<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (26)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (30)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (43)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (65)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 853
Ala Xaa Leu Ile Arg Xaa Arg Xaa Gly Xaa Ser Gln Ala Thr Leu Xaa

815

1 5 10 15
Val Thr Thr Thr Ser Thr Ser Tyr Arg Xaa Gln Pro Met Xaa Phe Val
20 25 30
Ile Xaa Phe Phe Ile Val Xaa Thr Leu Ile Xaa Gly Gly Phe Gly Gln
35 40 45
Leu Thr Ser Ser Leu Ile Met Gly Ala Pro Ile Trp Gly Leu Pro Ala
50 55 60
Xaa Asn Asn Ile Ser Phe
65 70

<210> 854
<211> 137
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<223> Xaa equals any of the naturally occurring L-amino acids

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<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (79)
 <223> Xaa equals any of the naturally occurring L-amino acids

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<220>
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<220>
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 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (130)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (133)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 854
 Pro Gln Ser Gln Gly Leu Xaa Pro Phe Gly Gln Xaa Xaa Val Lys Glu
 1 5 10 15
 Leu Asn Arg Xaa Gly Val Leu Ile Asp Leu Ala His Val Ser Val Ala
 20 25 30
 Thr Met Lys Ala Thr Leu Gln Leu Ser Arg Ala Pro Xaa Ile Phe Ser
 35 40 45
 His Ser Ser Ala Tyr Ser Val Cys Ala Ser Arg Arg Asn Val Pro Asp

817

50 55 60
 Asp Val Leu Arg Leu Val Lys Xaa Thr Asp Ser Leu Val Met Xaa Asn
 65 70 75 80
 Phe Tyr Asn Asn Tyr Ile Ser Cys Thr Asn Lys Ala Asn Leu Ser Gln
 85 90 95
 Val Ala Asp His Leu Asp His Ile Lys Glu Val Ala Xaa Ala Arg Xaa
 100 105 110
 Val Xaa Phe Gly Xaa Asp Phe Asp Gly Gly Pro Arg Val Pro Glu Xaa
 115 120 125
 Leu Xaa Asp Ala Xaa Ser Ile Gln Thr
 130 135

<210> 855
 <211> 84
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (20)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (31)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (74)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 855
 Gly Asp Ile Arg Ser Gly Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn
 1 5 10 15
 Cys Pro Thr Xaa Asp Gly Gly Trp Gln Val His Gly Val Thr Xaa Phe
 20 25 30
 Val Ser Ala Phe Gly Cys Asn Thr Arg Arg Lys Pro Thr Val Phe Thr
 35 40 45
 Arg Val Ser Ala Phe Ile Asp Trp Ile Glu Glu Thr Ile Ala Ser His
 50 55 60

Leu Glu Thr Lys Gly Pro Pro Trp Gln Xaa Leu Asn Arg Ser His Ile
 65 70 75 80

Leu Glu Ile Lys

<210> 856

<211> 117

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (106)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 856

Ala Arg Ala Gln Asn Asp Leu Glu Gln Val Leu Arg Gln Ile Gly Asp
 1 5 10 15

Lys Asp Gln Lys Ile Gln Asn Leu Glu Ala Leu Leu Gln Lys Ser Lys
 20 25 30

Glu Asn Ile Ser Leu Leu Glu Lys Glu Arg Glu Asp Leu Tyr Ala Lys
 35 40 45

Ile Gln Ala Gly Glu Gly Glu Thr Ala Val Leu Asn Gln Leu Gln Glu
 50 55 60

Lys Asn His Thr Leu Gln Glu Gln Val Thr Gln Leu Thr Glu Lys Leu
 65 70 75 80

Glu Glu Ser Val Arg Lys Phe Ile Asn Lys Pro Arg Glu Asn Leu His
 85 90 95

Gly Pro Gly Thr Arg Ala Glu Gly His Xaa Leu Glu Leu Ala Gln Asp
 100 105 110

Arg Val Pro Phe Pro
 115

<210> 857

<211> 62

<212> PRT

<213> Homo sapiens

<220>
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 <222> (2)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (3)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (9)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (15)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (16)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (45)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (50)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 857
 Gly Xaa Xaa Glu Ala Gln Thr Ser Xaa Pro Trp Asn Leu His Xaa Xaa
 1 5 10 15

His His Ser Leu Ser Pro Ile Val Leu Met Gly Ala Leu Xaa Phe Pro
 20 25 30

Val Pro Ser Phe Leu Pro Pro Gly Leu Pro Xaa Asn Xaa Ala Ala Tyr
 35 40 45

Ser Xaa Pro Lys Leu Arg Gly Ser Phe Pro Pro Ala Ser Leu
 50 55 60

<210> 858

<211> 133

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (119)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

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<222> (124)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (125)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (127)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (132)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (133)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 858

Asn Ser Ala Arg Gly Asp Lys Phe Phe Thr Ser His Asn Gly Met Gln
 1 5 10 15

Phe Ser Thr Trp Asp Asn Asp Asn Asp Lys Phe Glu Gly Asn Cys Ala
 20 25 30

Glu Gln Asp Gly Ser Gly Trp Trp Met Asn Lys Cys His Ala Gly His
 35 40 45
 Leu Asn Gly Val Tyr Tyr Gln Gly Gly Thr Tyr Ser Lys Ala Ser Thr
 50 55 60
 Pro Asn Gly Tyr Asp Asn Gly Ile Ile Trp Ala Thr Trp Lys Thr Arg
 65 70 75 80
 Trp Tyr Ser Met Lys Lys Thr Thr Met Glu Gly Lys Ser His Ser Thr
 85 90 95
 Asp Ser Gln Leu Glu Glu Gly Gln Gln His His Leu Gly Gly Ala Lys
 100 105 110
 Gln Val Arg Pro Glu His Xaa Ala Glu Thr Gly Xaa Xaa Ser Xaa Tyr
 115 120 125
 Pro Glu Gly Xaa Xaa
 130

<210> 859
 <211> 162
 <212> PRT
 <213> Homo sapiens

<400> 859
 Trp Ile Pro Arg Ala Ala Gly Ile Arg His Glu Glu Ser Gly Arg Lys
 1 5 10 15
 Val Gln Ser Gly Asn Ile Asn Ala Ala Lys Thr Ile Ala Asp Ile Ile
 20 25 30
 Arg Thr Cys Leu Gly Pro Lys Ser Met Met Lys Met Leu Leu Asp Pro
 35 40 45
 Met Gly Gly Ile Val Met Thr Asn Asp Gly Asn Ala Ile Leu Arg Glu
 50 55 60
 Ile Gln Val Gln His Pro Ala Ala Lys Ser Met Ile Glu Ile Ser Arg
 65 70 75 80
 Thr Gln Asp Glu Glu Val Gly Asp Gly Thr Thr Ser Val Ile Ile Leu
 85 90 95
 Ala Gly Glu Met Leu Ser Val Ala Glu His Phe Leu Glu Gln Gln Met
 100 105 110
 His Pro Thr Val Val Ile Ser Ala Tyr Arg Lys Ala Leu Asp Asp Met

822

115 120 125
 Ile Ser Thr Leu Lys Lys Ile Ser Ile Pro Val Asp Ile Ser Asp Ser
 130 135 140
 Asp Met Met Leu Asn Ile Ile Asn Ser Ser Ile Thr Thr Lys Gly Ile
 145 150 155 160
 Ser Arg

<210> 860
 <211> 89
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (73)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (87)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 860
 Arg Met Thr Ser Arg Lys Lys Val Leu Leu Lys Val Ile Ile Leu Gly
 1 5 10 15
 Asp Ser Gly Val Gly Lys Thr Ser Leu Met Asn Gln Tyr Val Asn Lys
 20 25 30
 Lys Phe Ser Asn Gln Tyr Lys Ala Thr Ile Gly Ala Asp Phe Leu Thr
 35 40 45
 Lys Asp Val Met Val Asp Asp Arg Leu Val Thr Met Gln Ile Trp Gly
 50 55 60
 His Ser Arg Thr Gly Thr Val Pro Xaa Ser Arg Cys Gly Leu Leu Gln
 65 70 75 80
 Arg Cys Lys Leu Leu Arg Xaa Gly Ile
 85

<210> 861
 <211> 40

823

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (4)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 861

Ile	Pro	Gly	Xaa	Ile	Xaa	Val	His	Thr	Arg	Phe	Gln	Met	Pro	Asp	Gln
1				5					10					15	

Gly	Ile	Thr	Ser	Ala	Asp	Asp	Phe	Phe	Gln	Gly	Thr	Lys	Ala	Ala	Leu
			20					25					30		

Ala	Gly	Gly	Thr	Thr	Met	Asn	His
		35				40	

<210> 862

<211> 123

<212> PRT

<213> Homo sapiens

<400> 862

Lys	His	Lys	Arg	Glu	Ile	Tyr	Asp	Arg	Tyr	Gly	Arg	Glu	Gly	Leu	Thr
1				5					10					15	

Gly	Thr	Gly	Thr	Gly	Pro	Ser	Arg	Ala	Glu	Ala	Gly	Ser	Gly	Gly	Pro
			20					25					30		

Gly	Phe	Thr	Phe	Thr	Phe	Arg	Ser	Pro	Glu	Glu	Val	Phe	Arg	Glu	Phe
		35				40						45			

Phe	Gly	Ile	Gly	Asp	Pro	Phe	Ala	Glu	Leu	Phe	Asp	Asp	Leu	Gly	Pro
	50					55					60				

Phe	Ser	Arg	Ala	Ser	Arg	Thr	Gly	Phe	Pro	Thr	Leu	Lys	Pro	Leu	Leu
65				70				75					80		

Tyr	Phe	Ser	Ser	Ser	Phe	Pro	Gly	His	Pro	Ile	Leu	Leu	Leu	Ile	Phe
			85					90					95		

Ser	Phe	Asn	Pro	Gly	Leu	Val	Leu	Ser	Leu	Cys	Phe	Tyr	Ser	Thr	Pro
			100					105					110		

Leu Ser Lys Glu Ala His Pro His Pro Lys Ser
 115 120

<210> 863
 <211> 99
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (77)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (80)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
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 <222> (88)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (91)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 863
 Arg Glu Met Leu Thr His Arg Asn Gly Leu Val Lys Lys Gly Lys Glu
 1 5 10 15

Gln Asn Thr Gln Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr
 20 25 30

Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu
 35 40 45

His Cys Thr Gly His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro
 50 55 60

Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys Leu Xaa Leu Ile Xaa
 65 70 75 80

Glu Pro Ile Pro His Pro Ser Xaa Ile Glu Xaa Pro Leu His Thr Lys
 85 90 95

Thr Phe Leu

<210> 864
<211> 99
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (40)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (47)
<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (58)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
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<222> (75)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (86)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 864
Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp Leu Pro Gly
1 5 10 15
Ala Glu Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala
20 25 30
Ser Val Gly Asp Arg Ile Thr Xaa Thr Cys Arg Ala Ser Gln Xaa Ile
35 40 45
Glu Asn Trp Leu Ala Trp Tyr Gln Gln Xaa Pro Gly Lys Pro Pro Lys
50 55 60
Leu Leu Leu Ile Ser Asp Ala Ser Ser Leu Xaa Ser Gly Val Pro Ser
65 70 75 80
Arg Phe Ser Gly Met Xaa Leu Gly Arg Asn Ser Leu Ser Pro Phe Pro

85

90

95

Ala Cys Ser

<210> 865

<211> 96

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (31)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (79)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (89)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (92)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (93)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 865

Val	Gln	Met	Gln	Val	Gln	Asp	Ile	Leu	Glu	Gln	Asn	Glu	Ala	Leu	Lys
1			5					10						15	

Ala	Gln	Ile	Gln	Gln	Phe	His	Ser	Gln	Ile	Ala	Ala	Gln	Thr	Xaa	Ala
		20						25					30		

Ser	Val	Leu	Ala	Glu	Glu	Leu	His	Lys	Val	Ile	Ala	Glu	Lys	Asp	Lys
		35						40					45		

Gln	Ile	Lys	Gln	Thr	Glu	Asp	Ser	Leu	Thr	Ser	Glu	Arg	Asp	Arg	Leu
		50				55						60			

Thr	Ser	Lys	Glu	Glu	Glu	Leu	Lys	Asp	Ile	Gln	Asn	Met	Asn	Xaa	Leu
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

827

65 70 75 80
Leu Lys Ala Glu Val Gln Lys Leu Xaa Ala Leu Xaa Xaa Glu Gln Ala
 85 90 95

<210> 866
<211> 79
<212> PRT
<213> Homo sapiens

<400> 866
Asp Tyr Arg Val His Ile Ile Ser Phe Lys Asp Pro Asn Pro Met His
1 5 10 15

Ile Asp Ala Thr Phe Asn Ile Ile Gly Pro Gly Ile Val Leu Ser Asn
 20 25 30

Pro Asp Arg Pro Cys His Gln Ile Asp Leu Phe Lys Lys Ala Gly Trp
 35 40 45

Thr Ile Ile Thr Pro Pro Thr Pro Ile Ile Pro Asp Asp His Pro Leu
 50 55 60

Trp Asp Val Ile Gln Met Ala Phe His Glu Cys Leu Asn Ala Arg
65 70 75

<210> 867
<211> 119
<212> PRT
<213> Homo sapiens

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<400> 867
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Gly Ile Pro Gly Ser Thr His Ala Ser Ala Trp Ala Arg Thr Xaa Pro
20 25 30

Arg Arg Arg Ala Xaa Gly Trp Gly Ala Xaa Trp Ala Arg Ser Gln Gly
35 40 45

Leu Asp Pro Thr Gly Pro Cys Xaa Xaa Asp Xaa Pro Glu Xaa Val Arg
50 55 60

Trp Xaa Pro Ser Xaa Ala Val Cys Val Asp Val Ile His Thr Tyr Ser
65 70 75 80

Ser Pro Ile Xaa Pro Pro Arg Cys Phe Arg Met Thr Gln Xaa Val Xaa
85 90 95

His Leu Asp Phe Xaa Pro Xaa Gly Arg Lys Asp Xaa Pro Xaa Val Lys
100 105 110

Xaa Cys Ser Xaa His His Xaa
115

<210> 868

<211> 178

<212> PRT

<213> Homo sapiens

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<400> 868

833

Gly Glu Thr Glu Gly Thr Gly Asp Ser Gly Leu Arg Ala Ala Pro Gly
 1 5 10 15
 Gly Leu Lys Asn Arg Arg Gln Pro Arg Arg Trp Ser Pro Ile Pro Gly
 20 25 30
 Tyr Ala Leu Gly Ser Glu Lys Ala Ala Ala Gly Gly His Ala Arg Gly
 35 40 45
 Gly Xaa Arg Gly Met Ala Ala Val Trp Gln Gln Val Leu Ala Val Asp
 50 55 60
 Ala Ser Phe Gly Arg Ser Ile Ser Ala Ala Gln Pro Ala Ala Ala Gly
 65 70 75 80
 Xaa Met Pro Arg Val Gly Thr Pro Ser Ala Ala Ser Gly Xaa Pro Glu
 85 90 95
 Ala Ser Gly Ala Xaa Cys Trp Ala Xaa Xaa Thr Xaa Pro Leu Xaa Xaa
 100 105 110
 Lys Glu Cys Ser Val Pro Ile Thr Thr Ala Ser Ser Gly Ser Xaa Arg
 115 120 125
 Thr Tyr Ser Xaa Xaa Gly Trp Lys Asp Xaa Gly Arg Xaa Ile Pro Xaa
 130 135 140
 Xaa Pro Xaa Gly Ala Arg Gly Ala Xaa Ser Phe Pro Phe Gln Lys Lys
 145 150 155 160
 Xaa Xaa Pro Xaa Xaa Gly Gly Gly Gly Xaa Xaa Xaa Asn Arg Gly Pro
 165 170 175
 Ser Xaa

<210> 869

<211> 38

<212> PRT

<213> Homo sapiens

<400> 869

Val Asn Pro Lys Tyr Ile Val Leu Glu Ser Asp Phe Thr Asn Asn Val
 1 5 10 15

Val Arg Cys Asn Ile His Tyr Thr Gly Arg Tyr Val Ser Ala Thr Asn
 20 25 30

Cys Lys Ile Val Gln Ser

834

35

<210> 870
<211> 119
<212> PRT
<213> Homo sapiens

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<222> (53)
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<400> 870
Gly Lys Lys Arg Gly Phe Ala Phe Val Thr Phe Asp Xaa His Asp Ser
1 5 10 15
Val Asp Lys Ile Val Ile Gln Lys Tyr His Thr Val Asn Gly His Asn
20 25 30
Cys Glu Val Arg Lys Ala Leu Ser Lys Gln Glu Met Ala Ser Ala Ser
35 40 45
Ser Ser Gln Arg Xaa Arg Ser Gly Ser Gly Asn Phe Gly Gly Gly Arg
50 55 60
Gly Ser Gly Phe Gly Gly Asn Asp Asn Phe Gly Arg Gly Gly Asn Phe
65 70 75 80
Ser Gly Arg Gly Gly Phe Gly Gly Ser Arg Gly Gly Gly Gly Tyr Gly
85 90 95
Gly Ser Gly Asp Gly Tyr Asn Gly Phe Gly Asn Asp Gly Ser Asn Phe
100 105 110
Gly Lys Trp Trp Lys Leu Gln
115

<210> 871
<211> 113
<212> PRT
<213> Homo sapiens

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<220>
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 <222> (112)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 871

Ala Arg Gly Thr Leu Leu Leu Ser Thr Leu Val Ala Gly Ala Leu Ser
 1 5 10 15

Cys Gly Val Ser Thr Tyr Ala Pro Asp Met Ser Arg Met Leu Gly Gly
 20 25 30

Glu Glu Ala Arg Pro Asn Ser Trp Pro Trp Gln Val Ser Leu Gln Tyr
 35 40 45

Ser Ser Asn Gly Gln Trp Tyr His Xaa Cys Gly Gly Ser Leu Asp Ser
 50 55 60

Gln Gln Leu Gly Pro Xaa Gly Cys Pro Leu His Gln Phe Leu Arg Asp
 65 70 75 80

Leu Pro Arg Gly Cys Trp Xaa Ser Met Asn Leu Leu Arg Trp Gln Ser
 85 90 95

Ser Gly Ser Leu Gly Leu Gln Cys Leu Xaa Arg Leu Leu Val Gln Xaa
 100 105 110

Gly

<210> 872
<211> 71
<212> PRT
<213> Homo sapiens

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<222> (30)
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<222> (67)
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<400> 872
Gly Ala Met Gln Glu Glu Leu Gln Trp Pro Phe Pro Ser Pro Gly Tyr
1 5 10 15
Leu Leu Tyr Ser Thr Gly His Arg Ala Gln Trp Arg Arg Xaa Glu Trp
20 25 30
Arg Ser Xaa Asp Val Met Asn Tyr Phe Ala Trp Glu Arg Asn Pro Ser
35 40 45
Thr Ile Ser Ser Pro Gly His Cys Ala Ser Leu Ser Arg Ser Thr Ala
50 55 60
Phe Leu Xaa Val Glu Arg Leu
65 70

<210> 873
<211> 79
<212> PRT
<213> Homo sapiens

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<222> (79)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 873

Ser	Arg	Gly	Ser	Asp	Pro	Phe	Leu	Glu	Tyr	Asn	Asn	Tyr	Gly	Cys	Tyr
1				5				10						15	

Cys	Gly	Leu	Gly	Gly	Ser	Ser	Thr	Pro	Val	Asp	Glu	Leu	Asp	Lys	Cys
	20						25						30		

Cys	Gln	Thr	His	Asp	Asn	Cys	Tyr	Asp	Gln	Ala	Lys	Xaa	Leu	Asp	Ser
	35						40					45			

Cys	Xaa	Phe	Leu	Leu	Asp	Asn	Pro	Tyr	Thr	His	Thr	Tyr	Ser	Tyr	Ser
	50					55					60				

Cys	Ser	Gly	Ser	Ala	Ile	Thr	Cys	Tyr	His	Gln	Lys	Gln	Xaa	Xaa
65					70					75				

<210> 874

<211> 41

<212> PRT

<213> Homo sapiens

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<222> (6)

<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (8)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (15)

<223> Xaa equals any of the naturally occurring L-amino acids

838

<400> 874

Arg Ser Gln Glu Tyr Xaa Arg Xaa Pro Ala Ala Arg Ser Ser Xaa Thr
1 5 10 15
Leu Trp Arg Ile Arg Thr Arg Leu Ser Leu Cys Arg Gly Pro Arg Ala
20 25 30
Ala Ala Ala Ala Leu Pro Pro Ala Cys
35 40

<210> 875

<211> 64

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (53)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (54)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 875

Gln Ser Pro Glu Ser Pro Arg Arg Val Gln Leu Gly Arg Phe Asp Arg
1 5 10 15
Arg Arg Glu Pro Asp Thr Asp Arg Ser Trp Arg Pro Phe Ser Leu Ser
20 25 30
Glu Cys Cys Ser Cys His Cys Gly His Gly Arg Tyr Pro Val Pro Val
35 40 45
Glu Val His Gly Xaa Xaa Thr Gly Arg Lys Leu Ala Lys Lys Ala Val
50 55 60

<210> 876

<211> 97

<212> PRT

<213> Homo sapiens

<400> 876

839

Ser Asp Arg Pro Thr Met Ala Pro Gly Val Ala Arg Gly Pro Thr Pro
1 5 10 15
Tyr Trp Arg Leu Arg Leu Gly Gly Ala Ala Leu Leu Leu Leu Leu Ile
20 25 30
Pro Val Ala Ala Ala Gln Glu Pro Pro Gly Ala Ala Cys Ser Gln Asn
35 40 45
Thr Asn Lys Thr Cys Glu Glu Cys Leu Lys Asn Val Ser Cys Leu Trp
50 55 60
Cys Asn Thr Asn Lys Ala Cys Leu Asp Tyr Pro Val Thr Ser Val Leu
65 70 75 80
Pro Pro Ala Ser Leu Cys Lys Leu Ser Ser Ala Arg Trp Gly Val Cys
85 90 95

Gly

<210> 877

<211> 54

<212> PRT

<213> Homo sapiens

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<400> 877

Ala Lys Xaa Arg Xaa Pro Arg Gln Ser Cys Leu Ile His Glu Ser Xaa
1 5 10 15

Cys Pro Glu Gly Thr Asn Ala Tyr Arg Ser Tyr Xaa Tyr Tyr Phe Asn
20 25 30

Glu Asp Pro Glu Thr Xaa Val Asp Ala Arg Ser Leu Leu Pro Glu His
35 40 45

Glu Phe Xaa Xaa Pro Gly
50

<210> 878

<211> 74

<212> PRT

<213> Homo sapiens

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<222> (68)

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<400> 878

His Tyr His Leu Leu Phe Tyr Ser Tyr Asn Asp Tyr Val Arg Glu Phe
1 5 10 15

His Asn Met Gly Pro Pro Pro Pro Trp Gln Gly Met Pro Pro Tyr Pro
20 25 30

Gly Met Glu Gln Pro Pro His His Pro Tyr Tyr Gln His His Ala Pro
35 40 45

Pro Pro Gln Ala His Pro Pro Tyr Ser Gly His His Pro Val Pro Xaa
50 55 60

Glu Ala Arg Xaa Arg Asp Lys Arg Ile Ser
65 70

<210> 879

<211> 138

<212> PRT

<213> Homo sapiens

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<222> (83)

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<222> (102)

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<223> Xaa equals any of the naturally occurring L-amino acids

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<222> (115)

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<223> Xaa equals any of the naturally occurring L-amino acids

<400> 879

Asn	Ser	Ala	Arg	Gly	Glu	Leu	Ala	Phe	Leu	His	Thr	Ser	His	Cys	Leu
1				5					10					15	

Ala	Ser	Gly	Glu	Val	Met	Ile	Ser	Ser	Leu	Gly	Asp	Val	Lys	Gly	Asn
			20						25				30		

Gly	Lys	Gly	Gly	Phe	Val	Leu	Leu	Asp	Gly	Glu	Thr	Phe	Glu	Val	Lys
	35						40					45			

Gly	Thr	Trp	Glu	Arg	Pro	Gly	Gly	Ala	Ala	Pro	Leu	Gly	Tyr	Asp	Phe
	50					55					60				

Trp	Tyr	Gln	Pro	Arg	His	Asn	Val	Met	Ile	Ser	Thr	Glu	Trp	Ala	Ala
65				70						75					80

Pro	Asn	Xaa	Leu	Arg	Asp	Gly	Phe	Asn	Pro	Ala	Asp	Val	Glu	Ala	Gly
			85						90					95	

Glu	Asn	Pro	Pro	Met	Xaa	Gln	Gln	Glu	Pro	Xaa	Gly	Leu	His	Xaa	Leu
		100						105					110		

Xaa	Phe	Xaa	Val	Pro	Asn	Leu	Ser	Thr	Pro	Thr	Ile	Xaa	Leu	Xaa	Ile
		115					120					125			

Gly	Pro	Arg	Xaa	Leu	Lys	Xaa	Gly	Trp	Pro
	130					135			

<210> 880

<211> 107

<212> PRT

<213> Homo sapiens

<400> 880

Gln	Arg	Asp	Phe	Phe	Arg	Thr	Ser	Lys	Lys	Met	Tyr	Pro	His	Arg	Pro
1				5					10					15	

843

Val Leu Met Val Ile Ser His Ala Ala Pro His Gly Pro Glu Asp Ser
 20 25 30
 Ala Pro Gln Tyr Ser Arg Leu Phe Pro Asn Ala Ser Gln His Ile Thr
 35 40 45
 Pro Ser Tyr Asn Tyr Ala Pro Asn Pro Asp Lys His Trp Ile Met Arg
 50 55 60
 Tyr Thr Gly Pro Met Lys Pro Ile His Met Glu Phe Thr Asn Met Leu
 65 70 75 80
 Gln Arg Lys Ala Cys Arg Pro Ser Cys Arg Trp Thr Thr Pro Trp Arg
 85 90 95
 Arg Phe Thr Thr Cys Trp Leu Arg Arg Ala Ser
 100 105

<210> 881

<211> 122

<212> PRT

<213> Homo sapiens

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<221> SITE

<222> (88)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 881

Met Ile Phe Asn Ala Glu Arg Val Gly Gly Leu Glu Glu Glu Arg Glu
 1 5 10 15
 Ser Val Gly Pro Leu Arg Glu Asp Phe Ser Leu Ser Ser Ser Ala Leu
 20 25 30
 Ile Gly Leu Leu Val Ile Ala Val Ala Ile Ala Thr Val Ile Val Ile
 35 40 45
 Ser Leu Val Met Leu Arg Lys Xaa Ala Val Trp His His Gln Pro Arg
 50 55 60
 Asp Arg Gly Gly Leu Ile Gln Cys Ser Pro Gln Lys Asn Val Pro Glu
 65 70 75 80

844

Gln Asp Ala Glu Pro Cys Tyr Xaa Asn Pro Leu Pro Ile Leu Asp Arg
85 90 95
Ser Ile Arg Leu Gln Asp Ala His Leu Arg Gly Ser Val Ala Glu Ile
100 105 110
His Ile Arg Ser Met Gln His Thr Val Gln
115 120

<210> 882

<211> 26

<212> PRT

<213> Homo sapiens

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<220>

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<222> (23)

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<400> 882

Phe Xaa Asn Gly His Gln Glu Lys Asn Xaa Phe Leu Ala Xaa Gln Gly
1 5 10 15

Pro Lys Glu Glu Thr Val Xaa Asp Phe Trp
20 25

<210> 883

<211> 34

<212> PRT

<213> Homo sapiens

845

<400> 883

Gln Ala Arg His Leu Leu Leu Gly Gln Arg Val Leu Val Leu Glu Leu
1 5 10 15

Ser Cys Glu Gly Asp Asp Glu Asp Thr Ala Phe Pro Thr Leu His Tyr
20 25 30

Glu Leu

<210> 884

<211> 35

<212> PRT

<213> Homo sapiens

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<400> 884

Gly Pro Ala Ser Pro His Ala Thr Leu Gly Pro Xaa Pro Cys Arg Val
1 5 10 15

Leu Phe Ser Met Ser Phe Ile Pro Xaa Xaa Glu Xaa Phe Arg Leu Pro
20 25 30

His Pro Gln

35

<210> 885

<211> 73

<212> PRT

<213> Homo sapiens

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<222> (66)

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<400> 885

Xaa Pro Xaa Met Ala Ser Val Val Leu Pro Ser Gly Ser Gln Cys Ala
1 5 10 15

Ala Ala Xaa Arg Arg Arg Arg Ser Arg Ala Pro Ala Pro Ala Ser Ala
20 25 30

Val Ala Leu Leu Arg Arg Gly Thr Glu Ser Pro Gln Val Met Gly Gln
35 40 45

Asn Leu Phe Thr Lys Arg Arg Asp Ser Asn Arg Gly Arg Gly Cys Glu
50 55 60

Pro Xaa Ser Cys Gln Val Asn Glu Glu
65 70

<210> 886

<211> 108

<212> PRT

<213> Homo sapiens

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<400> 886
 Asp Ser Pro Met Phe Xaa Trp Ser Glu Pro Pro Ser Cys Ser His Leu
 1 5 10 15
 His Cys Pro Ser Ala Leu Phe Val Pro Cys Xaa Xaa Lys Xaa Gly Ala
 20 25 30

Gln Met Val Arg Pro Glu Xaa Ala Ala Gly Gly Ile Trp Asp Thr Pro
35 40 45

Val Gly Thr Gly Cys Xaa Pro Gly Leu Ile Pro Ser Phe His His Asp
50 55 60

Arg Asn Ala Leu Xaa Lys Ala Gly Leu Leu Gly Ala Cys Ser Pro Arg
65 70 75 80

Pro Pro Gln Arg Glu Pro Arg Cys Phe Pro Xaa Pro His Pro Phe Pro
85 90 95

Xaa His Xaa Leu Thr Val Leu Leu Ala Gln Pro Glu
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<210> 887

<211> 77

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<400> 887

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Gly Gln Ser Thr Xaa Glu Pro Asp Ser Arg Thr Pro Gly Lys His Val
20 25 30

Gln Met Gln Leu Ser Leu Xaa Xaa Thr Asn Asn Ile Asp Pro Val Gly
35 40 45

Lys Asn Pro Asn Glu Thr Gln Gly Gly His Xaa Gly Gly His Leu Gly
50 55 60

Xaa Xaa Ser Asp Gly Xaa Ala Leu Gly Ala Xaa Thr Pro
65 70 75

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 Leu Gly Asp Cys Ala Trp Arg Trp Arg Arg Trp Arg Pro Leu Ala Ala
 20 25 30
 Gly Arg Ala Gln His Leu Xaa His Ala Arg Cys Glu Leu Xaa Xaa Ala
 35 40 45
 Glu Pro Gly Leu Arg Xaa
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<210> 889
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<400> 889
 Thr Ala Ser Ser Pro Gln Pro Ile Leu Leu Pro Leu Gln Pro Ala Glu
 1 5 10 15
 Glu Leu Ser Trp Ala Ala Pro Ile Ser Pro Asn Lys Val Tyr Ile Phe
 20 25 30

Cys Val Asp Ala Arg Pro Thr Ser Phe Pro Gly Phe Val Ala Val Arg
35 40 45

Arg Lys Gly His Glu Phe
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Ala His Ala Xaa Gly Xaa Xaa Gly Arg Arg Ser Lys Val Xaa Ile Phe
20 25 30
Phe Asp Gly Ser Arg Ser Ile Ser Leu Arg Lys Ser Lys Ile Asn Phe
35 40 45
Xaa Ser Arg Val Xaa Xaa Trp Phe
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<211> 57
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<400> 891
Ser Leu Val Pro Cys Pro Gln Ala Arg Trp Glu Ser Leu Gly Ser Ala
1 5 10 15
Tyr Ser Gly Ser Pro Leu Gly Ser Lys Gln Gly Gly Leu Ser Leu Pro
20 25 30
Glu Ser Asp Gly Arg Val Gly Gly Leu Gly His Leu Pro Val Pro Phe
35 40 45
Pro Lys Met Pro Ser Ser Val Pro Ala
50 55

<210> 892
<211> 73
<212> PRT
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<400> 892
Ser Thr His Ala Ser Val Cys Val Ala Tyr Ile Val Ala Gly Ala Trp
1 5 10 15
Leu Leu Ile Arg Ala Cys Thr Ser Phe Phe Asp Asn Lys Arg Val Lys
20 25 30
Ile Ala Pro Arg Pro Gly Glu Arg Glu Arg Val Ser Phe Tyr Ile Tyr
35 40 45
Ser Phe Gln Ala Asn Phe Gly Glu Ala Leu Thr Phe Leu Arg Gly Gly
50 55 60
Gly Gly Glu Val Lys Ser Cys Asp Leu

65

70

<210> 893

<211> 44

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<400> 893

Val Leu Gln Cys Pro Thr His Lys Asn Gly Lys His Gly Ser Leu Arg
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Leu Leu Gln Ser Thr Leu Leu Gln Ser Lys Ser Tyr Ser Leu Arg Lys
20 25 30

Cys Leu Leu Pro Phe Leu Phe Ser Ser Leu Leu Val
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<210> 894

<211> 56

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<400> 894

Ile Met Pro Ser Ser Ile Leu Ala Leu Gly Pro Thr Arg Pro Ser Ser
1 5 10 15

Asn Trp Glu Met Gly Arg Ser Lys Ala Gly Leu Met Leu Phe Arg Val
20 25 30

Ser Ser Tyr Leu Glu Leu Thr Arg Pro Thr Pro Val Ala Ile Pro Glu
35 40 45

Lys Ser Gln Leu Pro Gly Cys Leu
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 1 5 10 15

Xaa Asp Lys Xaa Xaa Leu Xaa Xaa His Arg Phe Xaa Ile Leu Lys Gln
 20 25 30

Met Xaa His Lys Val Arg Asp Ser Xaa Gly Xaa Ile Xaa Asp Lys Thr
35 40 45
Xaa Leu Asp Met Arg Val Tyr Gly Leu Arg Ala Xaa Val Leu Gly Leu
50 55 60
Glu Gln Gln Ile Ala Leu Met Cys Lys Pro Phe Asn Asn Ser Leu Phe
65 70 75 80
Arg Arg His Phe Phe Xaa Ala Lys Xaa Ser Trp Met Gln Xaa Xaa
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<210> 896

<211> 148

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Gly Cys Gln Xaa Leu Xaa Trp Thr Ser Trp Ser Xaa Arg Ser Xaa Arg

1

5

10

15

859

Val Cys Gln Ala His Leu Val Lys Lys Val Lys Met Gly Met Leu Val
20 25 30

Pro Trp Gly His Leu Val Leu Gln Xaa Gln Glu Val Leu Lys Val Pro
35 40 45

Met Glu Leu Met Asp His Lys Asp Pro Gln Gly Leu Phe Gly Ser Val
50 55 60

Gly Gly Val Gly Glu Lys Gly Glu Pro Gly Val Ser Arg Glu Pro Arg
65 70 75 80

Ala Ser Trp Gly Lys Gln Val Leu Gly Gly Pro Gln Ser Xaa Xaa Glu
85 90 95

Val Glu Lys Gly Gly Xaa Xaa Xaa Ser Thr Xaa Xaa Xaa Leu Gly Thr
100 105 110

Ser Gln Xaa Xaa Xaa Gly Xaa Thr Arg Xaa Cys Phe Gly Pro Lys Gly
115 120 125

Xaa Pro Gly Xaa Phe Xaa Val Phe Xaa Xaa Xaa Ser Gly Xaa Phe Gly
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Gly Phe Trp Xaa
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<210> 897

<211> 61

<212> PRT

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Ala Pro Gly Gln Xaa Gly Glu Ile Gly Pro Ser Gly Leu Thr Gly Xaa
1 5 10 15

Arg Xaa Phe Pro Gly Ser Pro Gly Xaa Xaa Gly Leu Pro Gly Ser Met
20 25 30

Gly Ser Pro Gly Thr Pro Ser Xaa Asp His Gly Xaa Thr Xaa Gly Pro
35 40 45

Gly Ile Val Gln Thr Ile Asp Asp Xaa His Cys Xaa Phe
50 55 60

<210> 898

<211> 37

<212> PRT

<213> Homo sapiens

<400> 898

Glu Gln Leu Lys Glu His Thr Arg Leu Cys Ser Lys Ile Val Gly Arg
1 5 10 15

Phe Ile Gly Arg Gly Asp Lys Pro Thr Glu Pro Gly Asp Ser Trp Leu
20 25 30

Ser Lys Ile Glu Ser
35

<210> 899

<211> 50

<212> PRT

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<400> 899

Asp Pro Gln Leu Ala Gly Gly Gln Ile Ser Arg Val Gly Gln Arg Gly
1 5 10 15

Lys Asn Ile Ala Ser Val Gly Asp Ala Val Gln Leu Pro Lys Gly Val
20 25 30

Arg Asn Gly Asn Ala Glu Xaa Trp Glu Lys Gly Ser Gly Gly Gly Arg
35 40 45

Arg Gly
50

<210> 900

<211> 53

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<213> Homo sapiens

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 Ile Ile Leu Ile Xaa Xaa Ser Leu Ser Lys Xaa Leu Gly Met Phe Ser . .
 1 5 10 15

Val Ile Gly Xaa Arg Tyr Gln Phe Pro Xaa Leu Ser Phe Asp Ile Gln
 20 25 30

Tyr Leu Ile Xaa Thr Leu His Xaa Trp Ser Ser Lys Xaa Xaa Leu Gln

35

40

45

Xaa Cys Gln Ile Ile
50

<210> 901

<211> 53

<212> PRT

<213> Homo sapiens

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<400> 901

Ala	Xaa	Arg	Val	Ser	Lys	Phe	Ser	Thr	Trp	Ile	Asn	Gln	Val	Ile	Ala
1				5					10				15		

Tyr	Asn	Xaa	Ala	His	His	Arg	Pro	Ser	Pro	Ala	Gln	Pro	Ile	Lys	Asp
			20					25					30		

Pro	Gly	Pro	Val	Pro	Ser	Cys	Ile	His	Val	Cys	Leu	Pro	Gly	Ser	Gly
		35					40						45		

Glu Arg Arg Gly Cys
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<210> 902

<211> 83

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 1 5 10 15
 Ser Phe Leu Leu Ser Ser Leu Leu Ala Leu Leu Thr Val Ser Thr Pro
 20 25 30
 Ser Trp Cys Gln Xaa Thr Glu Ala Ser Pro Lys Xaa Xaa Asp Gly Thr
 35 40 45
 Pro Phe Pro Trp Asn Lys Ile Arg Leu Pro Glu Tyr Val Ile Pro Val
 50 55 60
 Gln Tyr Lys Ser Leu Asp Xaa Cys Lys Pro Tyr Xaa Ala Asp Phe Trp
 65 70 75 80
 Gly Asn Xaa

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Gly Thr Ser Leu Lys Phe Phe Phe Leu Phe Lys Ile Leu Pro Gly Tyr
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Val Phe Ile Leu Ile Lys Phe Gly Cys Ser Xaa Ile Ser Leu Cys Lys
20 25 30

Xaa Thr Leu Ile Phe Ser Pro Lys Trp Asn Asp Glu Arg Phe Phe Ser
35 40 45

Pro Leu Pro Tyr Ala Pro Leu Lys Ser Tyr Met Ser Leu Tyr Tyr Leu
50 55 60

Ala Ile Met Gly Ile Phe Ile Ser Thr Val Val Leu Phe Trp Ser Ala
65 70 75 80

Pro Tyr Pro Val Asn Ile Ser Ile Val Leu Gln Xaa Leu Cys Ser Leu
85 90 95

Phe Cys Gln Gly Ser Xaa Val Xaa
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Gly Thr Ser Glu Phe Phe Xaa Phe Phe Phe Phe Phe Phe Phe Phe
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Phe Phe Phe Phe Xaa Phe Xaa Xaa
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<210> 905
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<212> PRT
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<400> 905
Gly Asn Lys Thr Leu His Leu Ile Pro Ile Thr Ser Ser Ile Ile Phe
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Gln Leu Ile Ile Lys Ser Val Leu Gly Asn Thr Leu Arg Thr Phe Met
20 25 30

Met Gln Gln Met Leu Thr Lys Gly Leu Val Gly Arg Tyr Ser Gly Asn
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Val His
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Glu Ile Trp Ser Ser Ile Leu Leu Arg Gln Gln Pro Xaa Glu Ser Asn
1 5 10 15

Leu Ser Leu Pro Ala Asp Asp Xaa Pro Ser Met Asn Arg Leu Gly Xaa
20 25 30

Gln Gln Val Pro Ser Phe Met Glu Leu Ser Leu Lys Asp Pro Xaa Val
35 40 45

Leu Lys Leu Xaa Gly Arg Xaa
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<210> 907

<211> 75

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 1 5 10 15

Pro Lys Gly Pro Ser Arg Glu Lys Asn Xaa Pro Gly Pro Gly Lys Lys
 20 25 30

Xaa Leu Gly Xaa Lys Xaa Arg Val Xaa Gly Ile Lys Arg Gly Xaa Xaa
 35 40 45

Leu Thr Phe Pro Pro Gly Phe Phe Pro Leu Gly Phe Ser Gln Lys Asn
 50 55 60

Phe Phe Pro Lys Gly Xaa Pro Lys Lys Ile Phe
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<210> 908

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<212> PRT

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Phe Phe Phe Gln Lys Tyr Val His Ile Xaa Ile Met Pro Lys Val Pro
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Pro Gly Xaa Val Lys Ala Arg Xaa Pro Gly Xaa Trp
 20 25

<210> 909
 <211> 141
 <212> PRT
 <213> Homo sapiens

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 Cys Leu Cys Pro Ala Pro Arg Gly Gly Ala Tyr Arg Gly Arg Gln Ala
 1 5 10 15

Ser Leu Ser Cys Gly Gly Leu His Pro Val Arg Ala Ser Trp Leu Leu
 20 25 30

Cys Leu Pro Lys Gln Ala Trp Ala Met Val Gly Ala Pro Pro Thr Ala
 35 40 45

Ser Leu Pro Pro Cys Ser Leu Ile Ser Asp Cys Cys Ala Ser Asn Gln
 50 55 60

Arg Asp Ser Met Gly Val Gly Pro Ser Glu Pro Gly Ala Gly Tyr Asn
 65 70 75 80

Leu Leu Val His His Ser Leu Ser Pro Ser Glu Lys His Ser Ile Arg
 85 90 95

Val Gly Val Thr Gln Phe Ser Arg Cys Arg Leu Ser Pro Leu Ser Leu
 100 105 110

Thr Arg Lys Gly Thr Ser Leu Thr Pro Cys Ala Ser Arg Val Lys Gln
 115 120 125

Cys Leu Asn Leu Leu Arg Leu Thr His Gly Gly Leu His
 130 135 140

<210> 910
 <211> 47
 <212> PRT
 <213> Homo sapiens

<400> 910
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 1 5 10 15

Ser Leu His Thr Cys Thr Gly Phe Pro Gln Tyr Leu Trp Ala Leu Val

871

20 25 30

Leu Gly Pro Leu Met Asp Thr Asn Ile Tyr Gly Cys Ser Ser Pro

35 40 45

<210> 911

<211> 84

<212> PRT

<213> Homo sapiens

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Met Gln Glu Leu Gly Phe Gln Pro Ser Leu Leu Thr His Trp Ala Ala

1 5 10 15

Gln Ser Ser Ala Ser Ser Ala Asp Ser Cys His Ser Leu Ala Gly Gly

20 25 30

Gly Pro Leu Val Phe His Thr Arg Val Lys Trp Ser Trp Cys Ser Leu

35 40 45

Ser Gly Val Leu Gly Trp Gly Ile Leu Cys His Xaa Gln Glu Arg Leu

50 55 60

His Leu Pro Val Ile Ser Pro Ala Pro Ser Val Pro Arg Gly Leu Pro

65 70 75 80

Gly Pro Gln Pro

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Gly	Trp	Leu	Ala	Gly	Glu	Val	Leu	Pro	Pro	Val	Xaa	Pro	Pro	Gly	Pro
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Xaa	Ser	Thr	Ser	Leu	Arg	Lys	Thr	Thr	Xaa	Pro	Xaa	Asp	Pro
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1				5				10						15	

Leu	Leu	Ser	Asn	Cys	Leu	Thr	Ala	Cys	Ser	Ser	His	Trp	Cys	Glu	Leu
			20				25					30			

Gln	His	Pro	Leu	Cys	Ser	Lys	Trp	Thr	Pro	Thr	Ala	Leu	Ala	Pro	Leu
		35					40					45			

873

Val Ala Pro Ala Arg Ala Pro Ala Pro Ala Ser Ala Xaa Ser Ala Asn
 50 55 60

Ala Pro Pro Ala Arg Arg Ala Ala Val Pro Ala Ala Pro Trp Ala Val
 65 70 75 80

Pro Ser Val Pro Arg Ala Ala Ser Ala Lys Gly His Xaa Lys Asn Ala
 85 90 95

Ala Ala Val Pro Asp Val Gly Thr Ala Leu Leu Pro Asp Val Asn Arg
 100 105 110

Thr Thr Cys Thr Thr Trp Ile Phe Leu Lys Ile Xaa His
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<210> 914

<211> 59

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 1 5 10 15

Ser Val Leu Pro Phe Val Ser Leu Leu Ile Leu Phe Leu Gly Gly Gly
 20 25 30

Xaa Phe Ala Phe Xaa Ser Ser Trp His Asn Phe His Phe Ile Leu Leu --
 35 40 45

Ser Val Tyr Xaa Asn Phe Pro Leu Ser Arg Leu
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874

<210> 915
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 1 5 10 15
 Val Ser Arg Trp Thr Arg Leu Pro Arg Ala Leu Ala Xaa His Leu Leu
 20 25 30
 Thr Gln Leu Arg Gly Phe Gly Ile Leu Trp Pro His Cys Glu Glu Ile
 35 40 45
 Gly Ser Gly Ser Glu Ala Thr Gly Arg Leu Pro Leu Pro Glu Ile Trp
 50 55 60
 Ser Glu Glu Xaa Pro Pro Ser Ser His His Ser Lys Glu Val His Glu
 65 70 75 80
 Asn Xaa Ser Val Ile Pro Phe Asn Xaa Val Asp Ile Thr Phe Ile
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<210> 916
 <211> 62
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1				5					10					15	

Val	Leu	Leu	Val	Ala	Ser	Cys	Gln	Glu	Ala	Asp	Asn	Ala	Gly	Ala	Ser
			20					25					30		

Leu	Leu	Val	Met	Leu	Arg	Leu	Leu	Gly	Gly	Phe	Gly	Val	Leu	Gly	Phe
		35					40					45			

Asn	His	Ser	Leu	Gln	Xaa	Ser	Thr	Phe	Tyr	Leu	Thr	Xaa	Xaa
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<211> 36

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Glu	Lys	Thr	Arg	Gln	Cys	Thr	Leu	Pro	Met	Xaa	Val	Ser	His	Asn	Thr
1					5				10				15		

Asp	Val	Thr	Phe	Ile	Cys	Phe	Ile	Ser	His	Leu	Val	Ser	Lys	Xaa	Phe
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

877

<210> 920

<211> 5

<212> PRT

<213> Homo sapiens

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5

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<211> 86

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<213> Homo sapiens

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cccgaaatat ctgccatctc aattag 86

<210> 922

<211> 27

<212> DNA

<213> Homo sapiens

<400> 922

gcggcaagct ttttgcaaag cctaggc 27

<210> 923

<211> 271

<212> DNA

<213> Homo sapiens

<400> 923

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gcccctaact cgcgccagtt cgcgccattc tccgccccat ggctgactaa ttttttttat 180

ttatgcagag gccgaggccg cctcggcctc tgagctattc cagaagtagt gaggaggctt 240

ttttggaggc ctaggctttt gcaaaaagct t 271

<210> 924

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<212> DNA

<213> Homo sapiens

<400> 924

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32

<210> 925

<211> 31

<212> DNA

<213> Homo sapiens

<400> 925

gcgaagcttc gcgactcccc ggatccgcct c

31

<210> 926

<211> 12

<212> DNA

<213> Homo sapiens

<400> 926

ggggactttc cc

12

<210> 927

<211> 73

<212> DNA

<213> Homo sapiens

<400> 927

gcggcctcga ggggactttc ccggggactt tccggggact ttccgggact ttccatcctg 60
ccatctcaat tag 73

<210> 928

<211> 256

<212> DNA

<213> Homo sapiens

<400> 928

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cagttccgcc cattctccgc cccatggctg actaattttt tttatttatg cagaggccga 180
ggccgcctcg gcctctgagc tattccagaa gtagtgagga ggcttttttg gaggcctagg 240
cttttgcaaa aagctt 256

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/05989

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/12, 1/21, 15/63

US CL : 536/23.5; 435/252.3, 320.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5; 435/252.3, 320.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Issued US Patents and Genbank sequence databases

search terms: SEQ ID NOS: 1-10

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database Genbank on STN. NCI-CGAP. 'National Cancer Institute, Cancer Genome Anatomy Project, Tumor Gene Index'. Accession No. AI302271, Posted 01 February 1999. (Relevant to SEQ ID NO:1)	1, 2, 5-10
X	Database Genbank on STN, GAO et al. 'Non-catalytic beta- and gamma-subunit isoforms of the 5'-AMP-activated protein kinase'. Accession No. U42412, Posted 30 May 1996. (Relevant to SEQ ID NO:2)	1, 2, 5-10

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

07 MAY 2000

Date of mailing of the international search report

19 JUL 2000

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
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Authorized officer

JOHN S. BRUSCA

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Form PCT/ISA/210 (second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/05989

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database Genbank on STN. ADAMS et al. 'Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequence'. Accession No. AA301420, Posted 18 April 1997. Nature, 377 (6547 suppl), 3-174 (1995). (Relevant to SEQ ID NO:3)	1, 2, 5-10
X	Database Genbank on STN, HILLIER et al. 'WashU-Merck EST Project 1977'. Accession No. AA447503, Posted 04 June 1997. (Relevant to SEQ ID NO:4)	1, 2, 5-10
X	Database Genbank on STN. NCI-CGAP. 'National Cancer Institute, Cancer Genome Anatomy Project Tumor Gene Index'. Accession No. AI090176, Posted 23 October 1998. (Relevant to SEQ ID NO:5)	1, 2, 5-10
X	Database Genbank on STN. ADAMS et al. 'Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequence'. Accession No. AA295211. Nature, 377 (6547 suppl), 3-174 (1995), Posted 18 April 1997.(Relevant to SEQ ID NO:6)	1, 2, 5-10
X	Database Genbank on STN, ADAMS et al. 'Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequence'. Accession No. AA295847. Nature, 377 (6547 suppl) 3-174 (1995). Posted 18 April 1997. (Relevant to SEQ ID NO:7)	1, 2, 5-10
X	Database Genbank on STN, ADAMS et al. 'Rapid cDNA sequencing (expressed sequence tags) from a directionally cloned human infant brain cDNA library'. Accession No. AA363715, Nature Genet. 4, 373-380 (1993). Posted 21 April 1997. (Relevant to SEQ ID NO:8)	1, 2, 5-10
X	Database Genbank on STN, CHEN et al. 'A transcriptional co-repressor that interacts with nuclear hormone receptors'. Accession No. U37146, Posted 31 October 1995. (Relevant to SEQ ID NO:9)	1, 2, 5-10
X	Database Genbank on STN, NOMURA. Accession No. D80010, Posted 10 July 1997. (Relevant to SEQ ID NO:10)	1, 2, 5-10

Form PCT/ISA/210 (continuation of second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/05989

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-12, 14, 15, 16, 21, and SEQ ID NO: 1-10

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/05989

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-12, 14, 15, 16, and 21, drawn to cDNA, polypeptides, genes, a method of using the cDNA to make host cells comprising the cDNA, and a method of making the polypeptide.

Group II, claim(s) 13, drawn to an antibody specific for the polypeptides of Group I.

Group III, claim(s) 17, drawn to a therapeutic method of using the cDNA or the polypeptide of Group I.

Group IV, claim(s) 18 and 19, drawn to a diagnostic method of using the cDNA or polypeptide of Group I.

Group V, claim(s) 20, drawn to a method of using the polypeptide of Group I to isolate a binding partner.

Group VI, claim(s) 22, drawn to a method of using the cDNA of Group I to identify the activity of the polypeptide encoded by the cDNA.

Group VII, claim 23, drawn to the binding partner made by the method of Group V.

The inventions listed as Groups I-VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: PCT Rule 13.1 and Annex B do not provide for unity of invention between two or more different products or methods of use that share a special technical feature.

In addition, each Group detailed above reads on distinct Groups drawn to multiple SEQ ID Numbers. The sequences are distinct because they are unrelated sequences, and a further lack of unity is applied to each Group. The lack of unity is partially waived and the Applicants must further elect 10 SEQ ID Numbers for examination in the elected Group detailed above.

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